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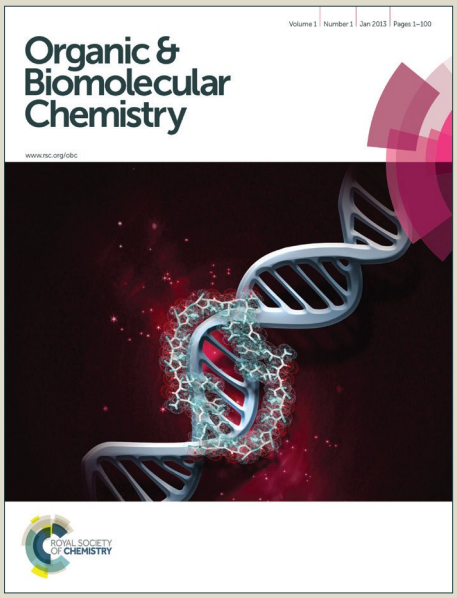

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ARTICLE

Regioselective vicinal functionalization of unactivated alkenes with sulfonium iodate(I) reagents under metal-free condition

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Dodla S. Rao,[a] Thurpu R. Reddy,[a] Kalvacherla Babachary[a] and Sudhir Kashyap*[a,b]

Metal-free, molecular iodine-free direct 1,2-difunctionalization of unactivated alkenes has been reported. The sulfonium iodate(I) reagent efficiently promoted the intermolecular vicinal iodo-functionalization of diverse range of olefins in stereo and regioselective manner. This method enables the divergent and straightforward preparation of synthetically useful functionalities; β-iodocarboxylates, β-iodohydrins, and β-iodoethers in one-step process. Further interconversion of iodo-functionalized derivatives allowing easy access to valuable synthetic intermediates en route for biologically active molecules.

Introduction

Stereoselective and divergent bisfunctionalization of alkenes has been recognised as an important transformation[1] to access versatile synthons en route for pharmaceutically valuable molecules and active natural products.[2] Recent progress in transition-metal catalysis led to rapid development of attractive and useful techniques for vicinal functionalization of alkenes.[3] Despite the significant advances and fascinating applications of transition-metals in organic chemistry,[4] use of these reagents are limited in large scale applications and active pharmaceutical ingredients.[5] The intrinsic drawbacks of transition-metal catalysts or heavy metal salts such as toxicity and use of expensive ligands, additive or co-catalysts, moisture sensitive and confront challenges in removal of metal residues, stimulate to achieving greener and sustainable chemistry.[6]

Particularly, halofunctionalization, also known as "cohalogenation" of alkenes, is widely studied[7] and elegant reaction enabled selective and facile addition of two new chemical entities in single step.[8] This process generally proceed through halogenium ion[9] which involves addition of electrophilic halide, for instance iodate (I^+), on olefin then subsequent opening of cyclic iodonium intermediate with nucleophile (solvent) stereospecifically generates 1,2-*trans*-cohalogenated products. Cohalogenation of alkenes introducing two stereocenters with exclusive anti selectivity to incorporate vicinal ester (β-iodoesters), hydroxy (β-iodohydrin), or alkoxy (β-iodoether) moieties have shown broad applications in organic chemistry as well in interdisciplinary fields.[10] Essentially, halofunctionalized substrates provide possibilities of further functional group transformations to access diverse and synthetically useful derivatives.

The iodocarboxylation of C=C double bond can be carried out by using molecular iodine[11a] as oxidant and electrophilic halogen source with metal salts (copper, silver, thallium, mercury, bismuth),[11b-c] or ammonium acetate.[11d] Other oxidizing reagent such as ceric ammonium nitrate (CAN),[11e] iodonium-di-sym-collidine perchlorate (IDCP),[11f] N-iodosuccinimide (NIS),[11g-h] potassium iodate (KIO_3),[11i-j] and hydrogen peroxide[11k] in acetic acid as the solvent also reported for similar transformations. Likewise, the iodoethers, represent useful synthetic intermediates for assembling *E*- or *Z*-alkenes,[12] are generally prepared via intermolecular cohalogenation of alkenes by employing iodonium source and alcohols.[13] In contrast, access to iodohydrin is generally difficult due to the possibility of reversible addition of iodine or hypoiodous acid (IOH generated *in situ*) on alkenes,[7a,14] hence co-oxidant as scavengers[15] or metal salts[16] such as $AgNO_3$, HgO, or $CuO.HBF_4$ are needed to trap the iodine ion. Alternatively, the epoxidation of alkenes by using peracids or peroxides, and subsequent ring-opening of oxirane ring with iodo-halides or metal-iodides provide the desired iodohydrin.[7a,13,17]

Notably, large scale preparation of epoxide derivatives[18] and biologically important oxiranes[19] predominantly relies on the practicability and efficiency of methods developed for halohydrin intermediates. However, excessive use of toxic oxidants and expensive metal salts, handling of halogenated reagents and formation of by-products such as vicinal dihalides or diols[20] and functional group compatibility of iodinating reagent system are associated limitations. Therefore, the developments of convenient and greener approaches for direct functionalization of alkenes utilizing metal-free and environmentally preferred reagents are highly desirable. In this

[a] *Department of Chemistry, Malaviya National Institute of Technology, Jaipur-302017, INDIA. E-mail: skashyap.chy@mnit,ac,in, skr.kashyap@gmail.com.*
[b] *INSPIRE Faculty, Department of Science and Technology (DST) and Assistant Professor, Academy of Scientific and Innovative Research (AcSIR), INDIA.*
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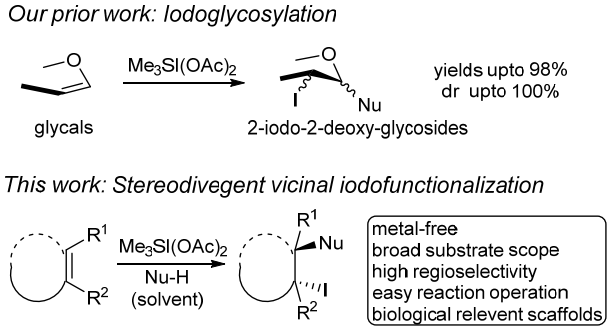
context, hypervalent iodine reagents are surged as versatile and attractive alternatives in vicinal bisfunctionalization of olefins.[21]

During our research towards glycochemistry,[22] we recently demonstrated the preparation of novel sulfonium bis(acetoxy)iodate(I) reagent and studied its utility in iodoglycosylation of glycals.[22a] The exceptional versatility of metal-free protocol highlighted for one-pot and divergent synthesis of glycosyl carboxylates and glycosyl azides in stereo- and regioselective manner. The efficiency and convenience of present reagent system encourage us to relate this method mechanistically for bisfunctionalization of unactivated C=C double bond (Scheme 1).



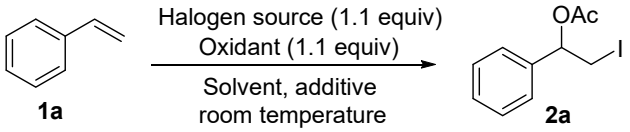
Scheme 1. Iodoglycosylation and rational for vicinal functionalization of alkenes with sulfonium bis(acetoxy)iodate (I) salt .

Herein, we present a facile approach for 1,2-cohalogenation of alkenes enabling the stereodivergent synthesis of vicinal iodoester, iodohydrin, and iodohydrin derivatives by employing sulfonium-salt based iodate(I) reagents. The operationally simple protocol is mild and promising alternative to toxic metal-based reagent system and applicable for a diverse range of olefins, switching the solvent system directed the intermolecular selective β-iodofunctionalization of double bond. Further transformations of β-iodo derivatives employs nucleophilic substitution with sodium azide allowing straightforward access to vicinal azido analogues, constitutes important sub unit with tremendous synthetic and biological applications.

Results and discussion

The sulfonium bis(acetoxy)iodate (I) [$Me_3SI(OAc)_2$], an active iodate(I) species to realize bisfunctionalization of C=C bond, could be generated *in situ* by employing phenyliodine(III)diacetate ($PhI(OAc)_2$) and trimethylsulfonium iodide (Me_3SI).[22a] We begin our studies with styrene (**1a**) as the model substrate, investigating the outcome of reaction under different condition by varying solvent, iodonium source, oxidants, additive, etc., results are illustrated in Table 1. Thus, treatment of a preformed solution of Me_3SI and $PhI(OAc)_2$ (1.1 equiv each) in CH_2Cl_2 with **1a** (1.0 equiv) at room temperature for 12 h led to the formation of exclusively a Markovnikov product, 2-phenyl-2-acetoxy-1-iodoethane (**2a**) in 56% yield with complete regioselectivity (entry 1).

Table 1. Screening and optimization of sulfonium bis(acetoxy)iodate (I) reagent system[a]



Entry	Iodo source	Oxidant/Additive	Solvent	Time	Yield[b]
1	Me_3SI	$PhI(OAc)_2$	CH_2Cl_2	12 h	56%
2	Me_3SI	$PhI(OAc)_2$	CH_3CN	12 h	78%
3	Me_3SI	$PhI(OAc)_2$	DCE	5 h	86%
4	Me_3SI	$PhI(OAc)_2$/4 Å MS	DCE	10 h	66%
5	Me_3SI	$PhI(OAc)_2$	AcOH	15 min	88%
6	Me_3SOI	$PhI(OAc)_2$	AcOH	1 h	82%
7	$Me_3SI(OAc)_2$	-	DCE	7 h	61%
8	$Me_3SI(OAc)_2$	-	AcOH	30 min	68%
9	Me_3SI	$NaIO_4$	AcOH	1 h	66%
10[c]	Me_3SI	H_2O_2	AcOH	24 h	traces
11[d]	Me_3SI	TBHP	AcOH	24 h	48%
12[e]	I_2	- /NH_4OAc	AcOH	15 min	82%[11a]
13[f]	NaI	$PhI(OAc)_2$/CBTAB	CH_2Cl_2	2 h	84%[8a]
14[g]	NH_4I	H_2O_2/Ac_2O	AcOH/ CH_3CN	1 h	67%[11f]

[a]Reaction conditions: **1a** (1.0 equiv), solvent (1 mL), 25 °C. [b]The isolated yields after column chromatography. [c]Reaction was performed with 35% aq H_2O_2. [d]70% aq TBHP was used. [e]Iodine (1.0 equiv), NH_4OAc (0.5 equiv). [f]NaI (1.0 equiv), $PhI(OAc)_2$ (2.0 equiv), CTAB (10 mol%). [g]NH_4I (1.2 equiv), 50% aq H_2O_2 (1.2 equiv).

Further screening employing acetonitrile and 1,2-dichloroethane as the solvent resulted improved yields, 78% and 86% respectively (entries 2,3). Attempt to conduct this experiment using 4Å molecular sieves led to a decreased yield (entry 4). In contrast, acetoxyiodonation of **1a** in acetic acid solvent to delivered the desired 1,2-iodoacetate **2a** in further increased yields (88%) albeit with shorter reaction time (entry 5). Moreover, switching the iodonium source to trimethylsulfoxonium iodide (Me_3SOI) or employing sulfonium bis(acetoxy)iodate (I) complex, $Me_3SI(OAc)_2$ directly, prepared by using our previously report,[22a] failed to improve the efficiency of the reaction (Table 1, entries 6-8). Apparently, presence of acetic acid as the solvent as well external nucleophile and *in situ* preparation of sulfonium iodate salt led to a better result. Further evaluation of other reagent such as $NaIO_4$, aq. H_2O_2, and TBHP as an alternative oxidant to PIDA resulted poor to moderate yields (entries 9-11).

Notably, the Woodward's reaction conditions utilizing molecular iodine,[11d] rather toxic, corrosive, and sublimable oxidant,[11a] provide lesser yields as compared to present

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protocol (entry 12). In contrast, use of other halide salt such as NaI in combination with $PhI(OAc)_2$ produce **2a** in 84% yield,[8a] however required twofold excess of oxidant and cetyltrimethylammonium bromide (CTAB) under critical concentration (entry 13). On the other hand, ammonium salt such as NH_4I as electrophilic iodine source and H_2O_2 as oxidant in the presence of Ac_2O in $AcOH/CH_3CN$ solvent system have been reported for oxidative iodoacetoxylation[11f] of styrene albeit with lower yield (entry 14).

Having established the optimized reaction conditions, the scope and general applicability of present protocol were examined for a wide range of electronically and sterically diverse olefins (Table 2). The styrene derivatives with electron-withdrawing groups for instance chloro-, fluoro- as well electron-donating substituents such as methyl-, *tert*-butyl-, and methoxy-, were reacted efficiently, affording the corresponding iodoacetates **2b-2f** in good yields (entries 1-5).

Furthermore, an electron rich 4-vinylbiphenyl, a highly substituted 2,4,6-trimethylstyrene, and 2-vinylnaphthalene preformed well to afford the desired products **2g**-**2i** respectively in good yields (entries 6-8). However, whereas α-Me styrene reacted smoothly yielding the corresponding iodoacetates **2j** in complete regioselectivity, diphenylethylene failed to produce **2k** in acceptable yield (entries 9,10). Encouraged by these results, we next investigated the influence of substituent's on β-position of terminal styrenes. Gratifying, *(E)*-β-methylstyrene underwent regio- and diastereoselective iodoacetoxylation to afford exclusive *trans* product (±)-3-acetoxy-2-iodo-3-phenylpropanoate (**2l**) in 90% yield (Table 2, entry 11). Subsequently, the stereoselective direct vicinal functionalization of α,β-unsaturated alkenes such as cinnamic acid (**1m**), methyl *trans*-cinnamate (**1n**), cinnamyl alcohol (**1o**), and cinnamyl acetate (**1p**) is accomplished successfully to obtain the desired products **2m-2p** in good yields (entries 12-15). In contrast, substrates with strong withdrawing groups at *β*-position in conjugation with double bond, for instance *trans*-cinnamaldehyde (**1q**) or *trans*-benzylidenacetone (**1r**), found to be challenging targets and failed to give satisfactory yield even after prolonged reaction time or at high temperature (entries 16,17).

On the other hand, internal aromatic olefins such as indene (**1s**) and 1,2-dihydronaphthalene (**1t**) were found to be compatible under these conditions. Accordingly, addition of electrophilic reagent on **1s** and **1t** resulted vicinal iodoacetates **2s-2t** with exclusive *trans*-diastereoselectivity and good yields (entries 18,19). It is pertinent to mention that, an aliphatic bicyclic alkene such as norborn-2-ene, produced 7-*syn*-iodo-2-exo-acetoxybicyclo[2.2.1]heptane (**2u**, entry 20), involving a distinct rearrangement of cationic intermediates as observed in previous reports[23] (Figure 1).

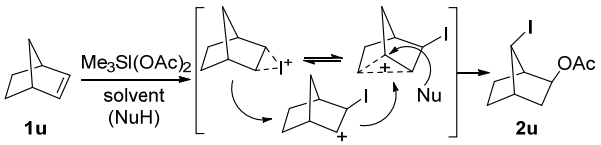
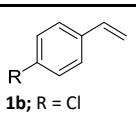
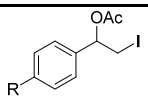
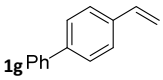
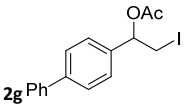
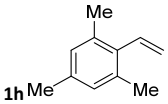
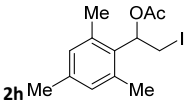
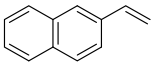
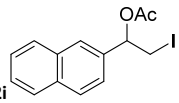
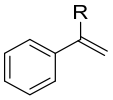
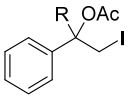
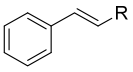
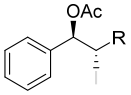
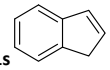
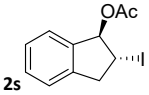
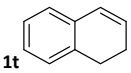
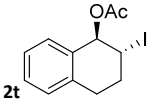
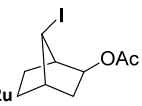


Figure 1. Probable rearrangement for norbornene iodofunctionalization

Table 2. Scope of metal-free iodoacetoxylation of alkenes with $Me_3SI(OAc)_2$ in one-pot[a]

Entry	Substrate	Product	Yield[b]
1	 **1b;** R = Cl	 **2b**; R = Cl	96%
2	**1c;** R = F	**2c**; R = F	84%
3	**1d;** R = Me	**2d**; R = Me	>99%
4	**1e;** R = *t*Bu	**2e**; R = *t*Bu	88%
5	**1f;** R = OMe	**2f**; R = OMe	85%
6	 **1g**	 **2g**	>99%
7	 **1h**	 **2h**	87%
8	 **1i**	 **2i**	92%
9	 **1j;** R = Me	 **2j**; R = Me	82%
10	**1k;** R = Ph	**2k**; R = Ph	traces
11	 **1l;** R = Me	 **2l**; R = Me	90%
12	**1m;** R = CO_2H	**2m**; R = CO_2H	>99%
13	**1n;** R = CO_2Me	**2n**; R = CO_2Me	87%
14	**1o;** R = CH_2OH	**2o**; R = CH_2OH	81%
15	**1p;** R = CH_2OAc	**2p**; R = CH_2OAc	98%
16	**1q;** R = CHO	**2q;** R = CHO	traces
17	**1r;** R = COPh	**2r**; R = COPh	traces
18	 **1s**	 **2s**	75%
19	 **1t**	 **2t**	94%
20	 **1u**	 **2u**	78%

[a]Reaction conditions: Substrate **1** (1.0 equiv), Me_3SI and $PhI(OAc)_2$ (1.1 equiv each), acetic acid (1 mL), 25 °C, 30-60 min. [b]The isolated and unoptimized yields after chromatography.

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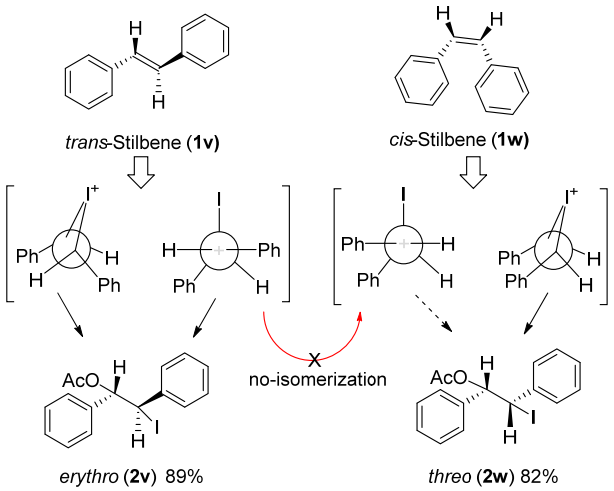
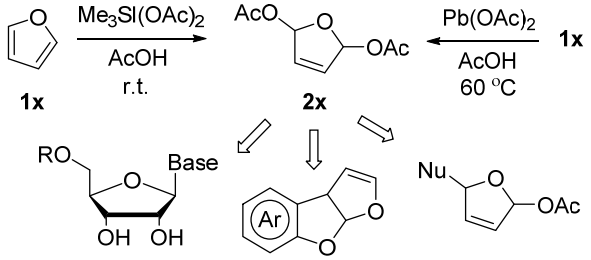
To further gain the mechanistic insight, we examined the addition of reactive species on *cis*/*trans* double bond. Assuming the *cis-trans* isomerization, *(E)*- and *(Z)*-stilbenes were chosen as mechanistic probes to realize the stereochemical outcome under present protocol (Scheme 2). Interestingly, reaction of *trans*-stilbene **1v** in acetic acid with sulfonium iodate(I) reagent generated *in situ* resulted the *erythro*-acetoxyiodide as a single diastereomer (±)-*trans*-2-iodo-1,2-diphenylethylacetate (**2v**). Despite the possibility of isomerization, iodoacetoxylation of *cis*-stilbene **1w** affording stereoselective *threo* product **2w**, attributed to stereospecific ring-opening of putative iodonium intermediate.[24] From mechanistic point of view, this transformation highlights a useful aspect of stereoselective (anti addition) vicinal bisfunctionalization of -C=C- double bond apart from regioselectivity (positional selectivity).



Scheme 2. Stereoselective preparation of β-iodocarboxylates from stilbenes *via* anti-addition and mechanistic illustration of *cis-trans* isomerization

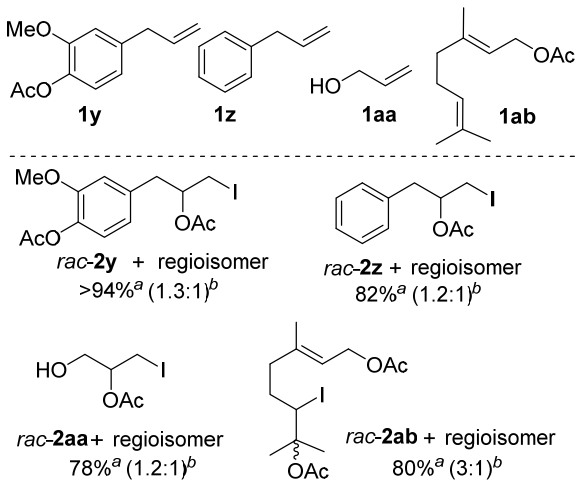
The stereochemistry of the product is unequivocally confirmed to be the *anti* addition and precisely correlated by spectroscopic analyses as well. In the ^{1}H NMR spectrum of *erythro* adduct, the characteristic resonances due to C*H*OAc and C*H*I are identified at δ 5.85 (d, *J* = 7.4 Hz) and 4.91 (d, *J* = 7.4 Hz) respectively. In contrast, *threo* configuration showed corresponding chemical shifts at slightly higher values at δ 6.17 and 5.33 with distinctive coupling constant, *J* = 9.8 Hz between α-protons. Notably, the formation of *erthro* and *threo* adduct in exclusive *anti*-diastereoselective manners is consistent with previous studies[24] and suggestive an ionic concerted one step process not a free radical one.

Next, it was of interest to examine the reactivity of electrophilic reagent on heterocyclic compound to expand the scope. Interestingly, the reaction of furan (**1x**), comprising a diene system with sulfonium bis(acetoxy)iodate (I) generated *in situ* delivered completely different adduct, 2,5-diacetoxy-2,5-dihydrofuran **2x** as 1:1 isomeric mixture in 90% overall yields (Scheme 3). Noteworthy, the scaffolds with 2,5-disubstituted dihydrofuran moiety are potential useful intermediates for several natural products and pharmaceutically fascinating molecules.[25] Despite the synthetic values of these structural motifs, a few scarce reports yet employs metal-based toxic reagent have been documented for their preparation.[25a] Therefore, our method offers an appealing and ideal-green synthesis of 2,5-diacetoxy-2,5-dihydrofuran albeit at room temperature.



Scheme 3. Synthesis of 2,5-diacetoxy-2,5-dihydrofuran and possible transformations to bioactive molecules. Reaction conditions: Furan (1.0 equiv), Me_3SI and $PhI(OAc)_2$ (1.1 equiv each), acetic acid (1 mL), 25 °C, 30 min.

We next explored the feasibility of non-conjugated olefin system and further evaluated the stereochemical information toward mechanistic studies. Interestingly, eugenol derivative (**1y**), substrate bearing an allylic moiety, yielded a mixture of regioisomers corresponding to Markovnikov and anti-Markovnikov-type products **2y** in good yields (Scheme 4). The lack of selectivity could be attributed to the variation of charge density on two carbons leading to non-regiospecifically ring opening of iodonium ion intermediate with acetate ion. Same trend of regioselectivity was observed in the electrophilic addition of less substituted terminal alkenes such as allylbenzene (**1z**) and allylalcohol (**1aa**), eliminating a free-radical pathway. In contrast, geraniol acetate undergo pronounced chemoselective iodoacetoxylation of terminal double bond to obtain notably better regioselectivity in favor of Markovnikov 1,2-iodoacetae **2ab** with a ratio of ~3:1 in 80% overall isolated yields.



Scheme 4. Scope of allylic double bond and mechanistic investigation: Substrate **1** (1.0 equiv), Me_3SI and $PhI(OAc)_2$ (1.1 equiv each), acetic acid (1 mL), 25 °C, 30-60 min. [a]The isolated and unoptimized yields after chromatography. [b]The ratio is based on ^{1}H NMR spectra.

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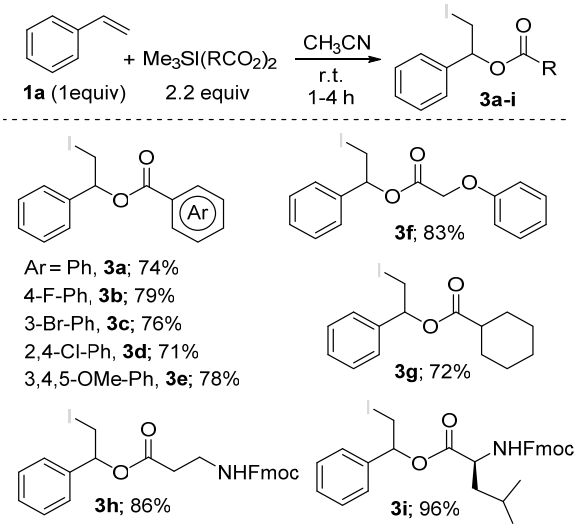
We next sought after developing carboxylic acid variant for the intramolecular hetero-functionalization by employing aryl, aliphatic, and amino acids. For this purpose, the reactive electrophilic intermediate, sulfonium bis(carboxy)iodate (I) complex prepared by using our previously described procedure,[22a] and utilized for iodocarboxylation step (Scheme 5). Initially, the reaction of styrene (**1a**) with $Me_3SI(OBz)_2$ in acetonitrile proceeded readily at ambient temperature affording the desired iodobenzoate **3a** in 74% isolated yield with absolute regioselectivity.[26a]

Subsequently, aromatic acids with halogen(s) at different position reacted smoothly to afford the corresponding products **3b**-**3d** in good yields (Scheme 5). Notably, an electron rich and highly substituted substrate such as 3,4,5-trimethoxybenzoic acid performed equally well to give **3e** in acceptable yield. Significantly, phenyl-ether bearing substrate, phenoxyacetic acid, which constitute organic herbicides and important chemical tools for clinical pharmacokinetics,[26b] was also tolerated under present protocol affording 2-iodo-phenoxyacetate product **3f** in 83% yield. In addition, alicyclic carboxylic acid was also suitable to obtain the corresponding β-iodocarboxylate **3g** in satisfactory yields.



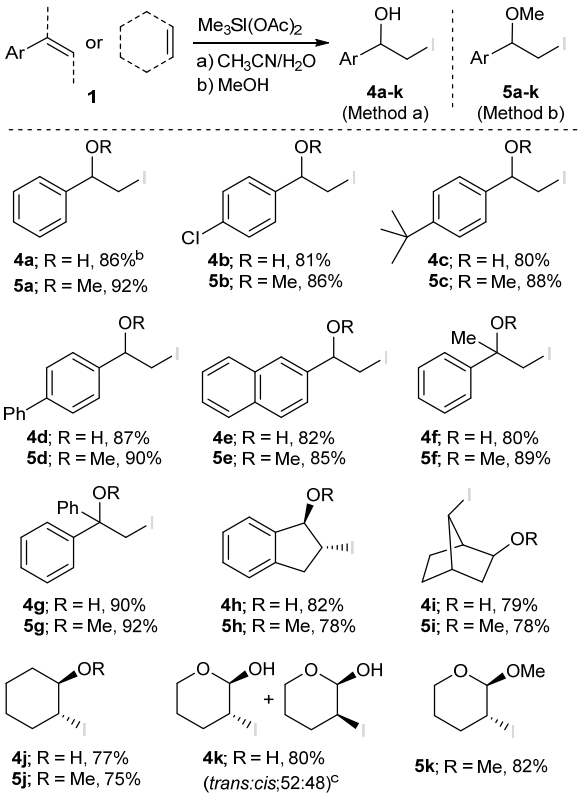
Scheme 5. Iodocarboxylaion of styrene: [a]Reaction conditions: Me_3SI and $PhI(OAc)_2$ (1.1 eq each), carboxylic acid (2.2 eq), CH_3CN (10 mL), 25 °C, 1 h, azeotroping off the acetic acid; (ii) CH_3CN (2 mL), **1a** (1.0 eq), 25 °C, 1-2 h.

Considering the biological significances of amino acid constructs, vicinal iodofunctionalization of **1a** with Fmoc-□-ala-OMe and Fmoc-L-leucine-OMe accomplished successfully by employing our reagent system to access the respective derivatives **3h**-**3i** in good yields.

We next investigated the possibility of further applications of sulfonium salt based iodate(I) reagent system in rapid and direct access of synthetically relevant iodofunctionalized compounds. We envisioned intramolecular version of hydroxy-iodonation of alkenes by employing water as the co-solvent as well alternative nucleophile to the acetic acid enabling iodohydrin adducts. To our delight, treatment of styrene (**1a**) with a solution of $Me_3SI(OAc)_2$ in acetonitrile-water (1:1) gives the corresponding iodohydrin **4a** in good yields (Scheme 6). Adopting this protocol, feasibility of various substituted aryl, and alicyclic alkenes were tested to extend the scope of the iodohydroxylation reaction.

As summarized in Scheme 6, styrene substrates with various functionalities (4-Cl, 4-*tert*-butyl, 4-phenyl), 2-vinylnaphthalene and α-methyl styrene reacted smoothly leading to the desired iodohydrins **4b**-**4f** in good yields with exclusive Markovnikov selectivity. Indeed, diphenylethylene being a challenging substrate, reacted this time to afford the iodohydrin derivative **4g** in satisfactory yields (Scheme 6). The versatility of sulfonium iodate(I) system was amply demonstrated in the anti-diastereoselective iodohydroxylation of indene and a few non-styrenyl substrates, such as norborn-2-ene, cyclohexnene (**1ac**) and dihydropyran (**1ad**). Nonetheless, bicyclo[2.2.1]heptene (**1u**) resulted the expected 2-*exo*,7-*syn*-stereoisomer (**4i**), the most obvious outcome of the ionic rearrangement as illustrated in Figure 1.

We next anticipated that switching the solvent system to methanol would enable to realize the synthesis of β-iodoethers in straightforward transformation. With sulfonium iodate (I) reagent in methanol (nucleophile) prepared *in situ* by employing a combination of Me_3SI and $PhI(OAc)_2$, a range of aryl, aryl-alkyl internal alkenes, bicyclic, endo-cyclic, and enol ether substrates were depicted to illustrate the stereoselective difunctionalization (**5a-k**, Scheme 6).



Scheme 6. Scope of $Me_3SI(OAc)_2$ mediated regio- and stereoselective iodofunctionalization in one-pot. [a]Reaction conditions: **1** (1.0 equiv), Me_3SI and $PhI(OAc)_2$ (1.1 equiv each), CH_3CN:H_2O (1:1; 1 mL) or MeOH (1 mL), 25 °C, 30-60 min. [b]The isolated yields after chromatography. [c]The ratio is based on ^1H NMR spectra.

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Overall, these results are consistent with the study and reveal the expected stereoselectivity for an ionic process; addition of electrophilc iodonium reagent from sterically less crowded face of the olefin following intramolecular diaxial nucleophilic opening of iodonium intermediate. Particularly, the protocol tolerates a diverse range of synthetically valuable functionalities establishing the vicinal functionalization of internal, terminal, and various substituted olefins stereo/regioselectively complementary to existing procedures.

The synthetic versatility of vicinal functionalized azides as valuable building blocks persuaded us to incorporate an azide group involving nucleophilic substitution of β-iodo prefunctionalized substrates. The resulting 1,2-azidoethers or azidoalcohols serve as useful precursor for aminoether, amino alcohol, aziridine, and heterocylic derivatives,[27] and represent an important structural motif for assembling active biomolecules as well approved drugs[28] (Figure 2).

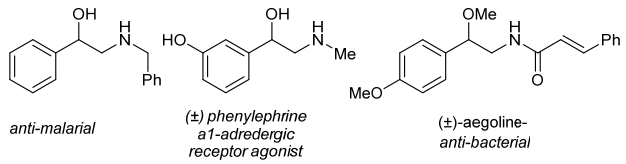
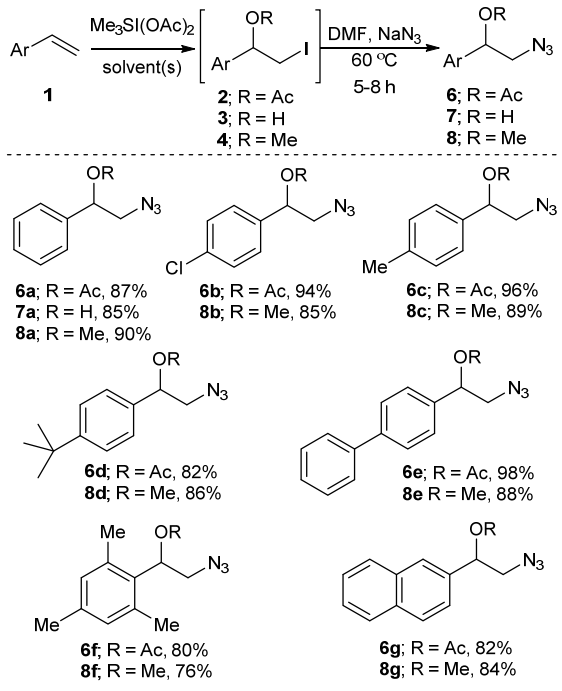


Figure 2. Biologically relevant molecules with 2-amino-1-phenyl scaffold

In this premise, we decided to synthesize β-azido from corresponding iodo compounds in a sequential one-pot process that employs vicinal iodofunctionalization of an alkene with our electrophilic reagent system following nucleophilic displacement with sodium azide (Scheme 7).



Scheme 7. Synthesis of β-azido derivatives in one-pot sequential process: [a]Reaction conditions: See footnote under Table 1. and Scheme 5. for the first step, then DMF (2 mL), NaN3 (1.5 equiv), 60 °C, 5-8 h.

In a representative example, the vicinal iodofunctionalization of styrene (**1a**) with electrophilic sulfonium iodate(I) were performed by employing acetic acid, acetonitrile:water, and methanol as the solvent(s) respectively. The resulting 2-iodo-1-phenylethyl analogs **2-4** were then directed to conventional iodo-azide transformation using sodium azide in DMF solvent at 50-60 °C to obtain the corresponding 2-azido-1-phenylethyl derivatives **6a-8a** in good yields.[29] Likewise, the sequential two steps transformation in one-pot applied to other styrene derivatives affording valuable functionalized azides in good yields, without isolation of the iodo-adducts (**6b-g**, **8b-g**, Scheme 7).

Additionally, the systematic modification of iodo group in heterofunctionalized derivatives provide rapid synthesis of analogues of some known drugs and structurally modified 'drug like' molecules of outmost therapeutic applications (Figure 3).[30] As illustrated in Scheme 8, incorporating a 1*H*-1,2,3-triazole moiety instead of imidazole in antifungal drugs such as miconazoles analogs by employing click reaction resulting a new class of antitubercular agents.[29b-c] Thus, iodoacetate **2a** prepared by *in situ* iodoacetoxylation step and subsequent "one-pot" nucleophilic substitution with benzotriazole employing DBU as the base in DMSO at room temperature for 8h afforded the corresponding amination product **9** in 78% yield over 2 steps (Scheme 8).

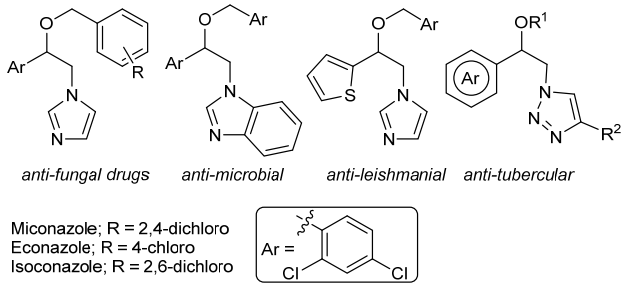
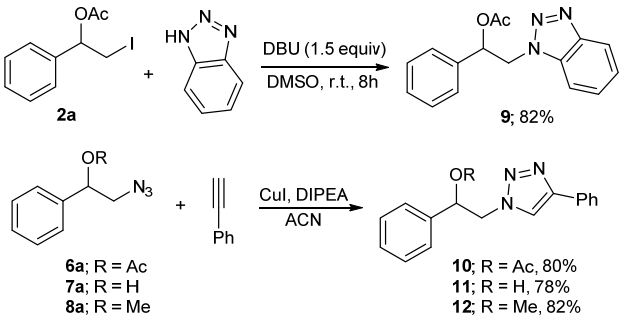


Figure 3. Pharmaceutical important imidazoles and triazole molecules.

In addition, β-azido compounds (**6a**,**7a**,**8a**), conveniently prepared from easily accessible starting material, were successfully coupled with phenylacetylene applying copper-catalyzed azide-alkyne cycloaddition (CuAAC) yielding the corresponding triazoles **10**-**12** in sequential transformation (Scheme 8).



Scheme 8. Transformations of iodofunctionalized product and rapid access to "drug-like" molecules.

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Conclusions

In conclusion, we have successfully demonstrated an intramolecular regio/stereoselective vicinal iodo-functionalization of alkenes. Employing sulfonium bis(acetoxy)iodate (I) species in different solvents allowing the facile and divergent synthesis of iodoester, iodohydrin, and iodoethers in a one-pot process. The scope and limitation of the electrophilic reagent system was illustrated with a wide range of structurally diverse olefins. The protocol is mild and tolerated various functionalities accessing synthetically useful heterofunctionalized derivatives under ambient conditions. The metal-free method utilizing easily available inexpensive and environmentally beings substrates/oxidants is potentially attractive and advantageous over the conventional methods. Importantly, diacetoxylation of furan is realized with sulfonium iodate(I) salt which further highlights a green approach avoiding stoichiometric use of toxic metal reagent. In addition, synthetic applicability of prefunctionalized β-iodo precursors was illustrated by simple organic transformations to access biologically significant scaffolds. Our investigations towards understanding mechanistic pathways employing sulfonium bis(acetoxy)iodate (I) species in new transformations and its applications in modern organic chemistry are currently in progress.

Experimental

General consideration: All reactions were performed in flame-dried round bottom flasks, fitted with rubber septa or glass gas adapters, under a positive pressure of nitrogen or argon. Removal of solvent under reduced pressure refers to distillation with a rotary evaporator attached to a vacuum pump (~3 mmHg). NMR were recorded on 300, 400 or 500 MHz nuclear magnetic resonance spectrometers. The proton resonances are annotated as: chemical shift (δ) relative to tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard or tetramethylsilane itself: chloroform-d (δ 7.26, singlet), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant (J, Hz), and number of protons for a given resonance is indicated by nH. The chemical shifts of ^{13}C NMR are reported in ppm relative to the central line of the triplet at 77.00 ppm for $CDCl_3$. High resolution mass analyses were performed on a mass spectrometer using ESI-TOF techniques.

Representative procedure for the synthesis of 1,2-iodoacetaes; A preformed solution of Me_3SI (237 mg, 1.16 mmol, 1.1 equiv) and $PhI(OAc)_2$ (374 mg, 1.16 mmol, 1.1 equiv) in 1 mL acetic acid was treated with alkene **1** (**1a**, 110 mg, 100 uL, 1.05 mmol, 1.0 equiv) at room temperature. After the completion of reaction, the reaction was diluted with EtOAc (10 mL), quenched with saturated $NaHCO_3$ (5 mL), saturated aqueous sodium thiosulfate (2 mL) and extracted with EtOAc (3 X 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography to obtain the desired β-iodoacetates or 2,5-diacetoxy-2,5-dihydrofuran. All the products were fully characterised by ^1H and ^{13}C spectroscopy and MS spectrometry and were in complete agreement with the assigned structure and correlated with literature data.

*Compound **2a**;*[13b] Oily liquid (271 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.30 (m, 5H), 5.88 (dd, *J* = 7.7, 5.5 Hz, 1H), 3.48 (dd, *J* = 10.6, 7.7 Hz, 1H), 3.45 (dd, *J* = 7.7, 2.7 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.77, 138.39, 128.71, 128.67, 126.38, 126.11, 75.16, 21.01, 7.73. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{10}H_{12}IO_2^+$: 290.98765; found: 290.98900. IR ($CHCl_3$, cm^{-1}): 2923, 1731, 1234, 699.

*Compound **2b**;*[13b] Oily liquid (293 mg, 96%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.46-7.18 (m, 4H), 5.82 (dd, *J* = 7.4, 5.6 Hz, 1H), 3.43 (m, 2H), 2.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.58, 137.42, 130.20, 128.86, 127.83, 74.39, 20.95, 7.26. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{10}H_{11}ClIO_2^+$: 323.94868; found: 323.95124. IR ($CHCl_3$, cm^{-1}): 2924, 1728, 1214, 747.

*Compound **2c**;* Oily liquid (208 mg, 84%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.31 (m, 2H), 7.07-7.03 (m, 2H), 5.84 (dd, *J* = 7.6, 5.6 Hz, 1H), 3.45 (dd, *J* = 10.6, 7.7 Hz, 1H), 3.42 (dd, *J* = 10.6, 5.6 Hz, 1H), 2.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.26, 163.21, 161.24, 134.01, 133.99, 128.01, 127.95, 116.28, 115.25, 115.07, 74.03, 20.53, 7.49, 1.37. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{10}H_{10}FIO_2^+$: 307.97095; found: 307.97225. IR ($CHCl_3$, cm^{-1}): 2923, 1732, 1216, 746.

*Compound **2d**;*[13b] Oily liquid (166 mg, 99%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.15 (m, 4H), 5.84 (dd, *J* = 7.9, 5.4 Hz, 1H), 3.46 (dd, *J* = 10.5, 8.5 Hz, 1H), 3.42 (dd, *J* = 10.5, 5.3 Hz, 1H), 2.33 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.68, 138.52, 135.38, 129.28, 126.29, 75.05, 21.16, 20.97, 7.82. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_2^+$: 303.99602; found: 303.99369. IR ($CHCl_3$, cm^{-1}): 2922, 1730, 1215, 754.

*Compound **2e**;* Oily liquid (218 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 5.87 (dd, *J* = 8.2, 5.1 Hz, 1H), 3.46 (dd, *J* = 10.5, 8.1 Hz, 1H), 3.43 (dd, *J* = 10.5, 5.1 Hz, 1H), 2.12 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.46, 151.42, 135.23, 125.94, 125.39, 74.85, 34.42, 31.12, 20.86, 7.76. HRMS (ESI) *m/z* $[M + NH_4]^+$ calcd. for $C_{14}H_{28}INO_2^+$: 364.07680; found: 364.07555. IR ($CHCl_3$, cm^{-1}): 2925, 1729, 1214, 750.

*Compound **2f**;*[13b] Oily liquid (202 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.4 Hz, 2H), 6.88 (d, *J* = 7.8 Hz, 2H), 5.87-5.80 (m, 1H), 3.79 (s, 3H), 3.51-3.36 (m, 2H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.64, 159.66, 130.34, 127.69, 113.88, 74.82, 55.15, 20.94, 7.90. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_3^+$: 319.99094; found: 319.99236. IR ($CHCl_3$, cm^{-1}): 2925, 1724, 1214, 748.

*Compound **2g**;* Oily liquid (203 mg, 99%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67-7.46 (m, 4H), 7.46-7.38 (m, 5H), 5.92 (dd, *J* = 7.8, 5.5 Hz, 1H), 3.50 (dd, *J* = 10.5, 7.8 Hz, 1H), 3.47 (dd, *J* = 10.5,

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5.3 Hz, 1H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.71, 141.57, 140.32, 137.26, 128.74, 127.47, 127.34, 127.01, 126.79, 74.92, 20.98, 7.60. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{16}H_{15}IO_2^+$: 366.01167; found: 366.00956. IR ($CHCl_3$, cm^{-1}): 2923, 1730, 1216, 759.

Compound ***2h****;*[13b] Oily liquid (219 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 2H), 6.32 (dd, *J* = 10.2, 5.1 Hz, 1H), 3.66 (t, *J* = 10.4 Hz, 1H), 3.41 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.42 (s, 6H), 2.23 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.41, 137.77, 137.23, 136.20, 131.05, 130.02, 72.80, 20.68, 20.62, 20.37, 4.75. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{13}H_{18}IO_2^+$: 333.03460; found: 333.03702. IR ($CHCl_3$, cm^{-1}): 2921, 1741, 1232, 742.

Compound ***2i****;*[13b] Oily liquid (204 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85-7.81 (m, 4H), 7.52-.7.46 (m, 2H), 7.42 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.04 (dd, *J* = 8.0, 5.3 Hz, 1H), 3.56 (dd, *J* = 10.5, 7.9 Hz, 1H), 3.52 (dd, *J* = 10.5, 5.1 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.73, 135.61, 133.25, 132.95, 128.59, 128.04, 127.67, 126.44, 125.97, 123.55, 75.28, 21.01, 7.60. HRMS (ESI) *m/z* $[M + Na]^+$ calcd. for $C_{14}H_{13}INaO_2^+$: 362.98524; found: 362.98401. IR ($CHCl_3$, cm^{-1}): 2924, 1739, 1229, 1048, 771, 748.

Compound ***2j****;*[11d] Semi solid (211 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.18 (m, 5H), 3.81 (m, 2H), 2.13 (s, 7H), 1.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.33, 141.79, 128.41, 127.64, 124.54, 80.72, 26.10, 21.98, 17.26. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_2^+$: 303.99602; found: 303.99398. IR ($CHCl_3$, cm^{-1}): 2960, 2924, 1733, 1447, 1028, 766, 699.

Compound ***2l****;* Yellow oily liquid (231 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.31 (m, 5H), 5.86 (d, *J* = 5.6 Hz, 1H), 4.53-4.30 (m, 1H), 2.14 (s, 3H), 1.83 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.34, 137.38, 128.28, 128.13, 126.82, 79.01, 28.05, 22.88, 20.82. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_2^+$: 303.99219; found: 303.99407. IR ($CHCl_3$, cm^{-1}): 2924, 2854, 1742, 1454, 1228, 1020.

Compound ***2m****;*[13c] Semi solid (113 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.32 (m, 5H), 6.87 (s, 1H), 6.17 (d, *J* = 10.8 Hz, 1H), 4.68 (d, *J* = 10.8 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.47, 168.93, 136.32, 129.31, 128.52, 128.03, 76.68, 21.89, 20.70. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{11}IO_4^+$: 339.97020; found: 339.96895. IR ($CHCl_3$, cm^{-1}): 3460, 3029, 2923, 1731, 1232, 1024, 753, 692.

Compound ***2n****;*[11j] Semi solid (94 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.34 (m, 5H), 6.14 (d, *J* = 10.7 Hz, 1H), 4.64 (d, *J* = 10.7 Hz, 1H), 3.80 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.76, 168.61, 136.50, 129.14, 128.40, 127.94, 76.64, 53.05, 22.39, 20.63. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{12}H_{14}IO_4^+$: 348.99313; found: 348.99541. IR ($CHCl_3$, cm^{-1}): 2924, 1735, 1734, 1215, 753.

Compound ***2o****;*[11j] Semi solid (375 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H), 4.91 (d, *J* = 5.2 Hz, 1H), 4.63-4.39 (m, 2H), 4.23 (dd, *J* = 11.4, 4.7 Hz, 1H), 2.87 (brs, 1H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.61, 140.15, 128.40, 128.31, 126.45, 75.64, 65.41, 36.24, 20.73. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_3^+$: 319.99094; found: 319.98895. IR ($CHCl_3$, cm^{-1}): 3482, 2924, 1737, 1233, 701.

Compound ***2p****;* Semi solid (193 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.28 (m, 5H), 5.95 (d, *J* = 6.3 Hz, 1H), 4.58 (dd, *J* = 12.2, 6.2 Hz, 1H), 4.51 (dd, *J* = 11.9, 6.3 Hz, 1H), 4.16 (dd, *J* = 11.9, 5.8 Hz, 1H), 2.14 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.51, 169.53, 137.39, 128.78, 128.42, 127.12, 75.35, 65.48, 30.64, 20.93, 20.75. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{13}H_{16}IO_4^+$: 363.00878; found: 363.01025. IR ($CHCl_3$, cm^{-1}): 2923, 2851, 1744, 1456, 1224, 1116.

Compound ***2s****;*[21a] Oily liquid (199 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.27 (m, 4H), 6.38 (d, *J* = 3.6 Hz, 1H), 4.48 (ddd, *J* = 6.8, 4.4, 3.7 Hz, 1H), 3.74 (dd, *J* = 17.0, 6.7 Hz, 1H), 3.33 (dd, *J* = 17.0, 4.5 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.34, 142.00, 138.51, 129.55, 127.49, 125.72, 124.69, 85.60, 43.32, 24.17, 20.94. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{11}IO_2^+$: 301.98037; found: 301.97852. IR ($CHCl_3$, cm^{-1}): 2922, 1729, 1460, 748.

Compound ***2t****;* Oily liquid (229 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.15 (m, 4H), 6.20 (d, *J* = 4.2 Hz, 2H), 4.63-4.50 (m, 1H), 3.06-2.96 (m, 1H), 2.94-2.85 (m, 1H), 2.35-2.10 (m, 2H), 2.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.89, 135.77, 131.28, 129.96, 128.77, 128.66, 126.41, 74.47, 28.41, 27.77, 27.69, 21.07. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{12}H_{13}IO_2^+$: 315.99602; found: 315.99850. IR ($CHCl_3$, cm^{-1}): 2924, 1697, 1449, 737.

Compound ***2u****;*[23b] Oily liquid (233 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (ddd, *J* = 7.7, 3.7, 1.1 Hz, 1H), 3.76 (t, *J* = 1.3 Hz, 1H), 2.59 (d, *J* = 3.3 Hz, 1H), 2.44 (m, 1H), 2.22-1.89 (m, 1H), 2.06 (s, 3H), 1.96 (ddd, *J* = 13.6, 7.7, 1.4 Hz, 1H), 1.64 (ddd, *J* = 18.1, 11.3, 7.8 Hz, 1H), 1.60- 1.14 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.70, 76.90, 47.77, 43.81, 38.61, 27.77, 25.21, 25.00, 21.31. IR ($CHCl_3$, cm^{-1}): 2924, 2853, 1742, 1459, 1259, 1139.

Compound ***2v****;* Semi solid (91 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.08 (m, 10H), 5.85 (d, *J* = 7.4 Hz, 1H), 4.91 (d, *J* = 7.4 Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.16, 139.02, 137.24, 136.81, 128.61, 128.10, 128.05, 127.98, 127.55, 127.20, 126.96, 126.44, 80.01, 77.00, 21.09. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{16}H_{15}IO_2^+$: 366.01167; found: 366.00985. IR ($CHCl_3$, cm^{-1}): 2926, 1731, 1232, 753.

Compound ***2w****;* Semi solid (167 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.02 (m, 5H), 6.16 (d, *J* = 9.9 Hz, 1H), 5.33 (d, *J* = 9.8 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.53, 139.56, 136.52, 128.50, 128.35, 128.28, 128.21, 127.10, 79.12, 35.68, 21.26. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{16}H_{16}IO_2^+$: 367.01895; found: 367.01636. IR ($CHCl_3$, cm^{-1}): 2923, 1735, 1372, 1233, 1052, 769, 699.

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*Compound **2x**;*[25b] Oily liquid (498 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.77 (s, 1H), 6.26 (s, 1H), 6.23 (s, 1H), 2.12 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.88, 169.74, 131.26, 130.86, 101.44, 99.97, 21.04, 20.94. IR ($CHCl_3$, cm^{-1}): 3107, 2926, 2853, 1749, 1748, 1367, 1230, 1099, 987, 814.

*Compound **2y**;* Semi solid (90 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, *J* = 6.1 Hz, 1H), 6.96 (d, *J* = 6.1 Hz, 1H), 6.86 (d, *J* = 1.7 Hz, 1H), 6.82 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.80 (d, *J* = 1.7 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.92-4.74 (m, 1H), 4.44-4.30 (m, 2H), 4.31-4.23 (m, 1H), 3.88-3.80 (m, 1H), 3.83 (s, 3H), 3.83 (s, 3H), 3.35 (dd, *J* = 10.7, 4.9 Hz, 1H), 3.25-3.15 (m, 2H), 2.98 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.94 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.31 (s, 6H), 2.10 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.11, 169.92, 168.82, 150.89, 138.58, 137.30, 134.88, 130.11, 127.33, 122.69, 122.64, 121.41, 120.98, 113.34, 113.01, 72.44, 68.27, 55.77, 43.05, 39.64, 28.96, 20.93, 20.67, 20.54, 7.68. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{14}H_{18}IO_5^+$: 393.01934; found: 393.02212. IR ($CHCl_3$, cm^{-1}): 3396, 3020, 2959, 1710, 1220, 1040, 752.

*Compound **2z**;*[11c] Oily liquid (239 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.17 (m, 10H), 4.88 (tt, *J* = 6.5, 5.0 Hz, 1H), 4.38 (m, 1H), 4.33 (dd, *J* = 11.7, 5.9 Hz, 1H), 4.26 (dd, *J* = 11.6, 6.2 Hz, 1H), 3.33 (dd, *J* = 10.7, 4.9 Hz, 1H), 3.27 (dd, *J* = 14.4, 6.5 Hz, 1H), 3.22-3.16 (m, 2H), 3.00 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.95 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.10 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.13, 169.91, 138.44, 137.34, 136.04, 130.13, 129.29, 128.84, 128.49, 128.47, 126.94, 126.85, 72.74, 68.29, 43.13, 39.86, 20.95, 20.73, 7.66. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{11}H_{13}IO_2^+$: 303.99602; found: 303.99923. IR ($CHCl_3$, cm^{-1}): 3482, 2924, 2853, 1737, 1223, 1017, 700.

*Compound **2aa**;* Oily liquid (388 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.86 (dd, *J* = 8.2, 3.1 Hz, 1H), 4.48 (dd, *J* = 11.8, 5.2 Hz, 1H), 4.36 (dd, *J* = 11.8, 7.0 Hz, 1H), 4.33-4.25 (m, 1H), 3.89-3.76 (m, 4H), 3.40 (dd, *J* = 10.5, 6.1 Hz, 1H), 3.32 (dd, *J* = 10.5, 5.6 Hz, 1H), 2.13 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.16, 170.96, 69.25, 66.95, 65.44, 64.80, 60.39, 31.02, 21.03, 20.77, 14.17, 8.82. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_5H_{13}INO_3^+$: 261.99346; found: 261.98005. IR ($CHCl_3$, cm^{-1}): 3394, 2923, 1719, 1227, 1017.

*Compound **2ab**;* Oily liquid (158 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (td, *J* = 7.0, 1.2 Hz, 1H), 4.69 (dd, *J* = 11.2, 2.3 Hz, 1H), 4.59 (d, *J* = 7.3 Hz, 2H), 2.47-2.35 (m, 1H), 2.06 (s, 3H), 2.02 (s, 3H), 2.12-1.74 (m, 1H), 1.71 (s, 3H), 1.65 (s, 3H), 1.58 (s, 3H), 1.20 (d, *J* = 2.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.04, 170.15, 140.83, 140.20, 119.68, 119.06, 83.01, 80.40, 61.14, 45.48, 39.58, 32.83, 25.88, 23.19, 22.29, 21.01, 16.43. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{14}H_{23}IO_4^+$: 382.06410; found: 382.06621. IR ($CHCl_3$, cm^{-1}): 2926, 2855, 1739, 1370, 1235, 1024.

Representative procedure for the synthesis of 1,2-iodocarboxylates; An equimolar mixture of Me_3SI (237 mg, 1.16 mmol, 1.1 equiv) and $PhI(OAc)_2$ (374 mg, 1.16 mmol, 1.1 equiv) in 10 mL CH_3CN was treated with carboxylic acid (BzOH, 284 mg, 2.32 mmol, 1.1 equiv) at room temperature. The reaction mixture was stirred at room temperature for 1 h. After evaporation of solution and dried on vacuum, to ensure the complete removal of acetic acid, the resulting residue were re-dissolved in CH_3CN (2 mL) and treated with **1a** (110 mg, 100 uL, 1.05 mmol, 1.0 equiv). After the completion of reaction, adjudged by TLC, the reaction was diluted with EtOAc (10 mL), quenched with saturated $NaHCO_3$ (5 mL), saturated aqueous sodium thiosulfate (2 mL) and extracted with EtOAc (3 X 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography to obtain the desired β-iodocarboxylates (**3a-3i**) in good yields..

*Compound **3a**;*[26a] White solid (278 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18-8.03 (m, 2H), 7.65-7.32 (m, 8H), 6.10 (dd, *J* = 7.7, 5.1 Hz, 1H), 3.62 (dd, *J* = 10.6, 7.7 Hz, 1H), 3.58 (dd, *J* = 10.6, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.33, 138.78, 133.28, 130.18, 129.82, 129.29, 128.71, 128.45, 126.29, 75.50, 8.02. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{15}H_{14}IO_2^+$: 353.00330; found: 353.00526. IR ($CHCl_3$, cm^{-1}): 2926, 2853, 1749, 1367, 1230, 1099, 987, 814.

*Compound **3b**;*[26a] Oily liquid (310 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18-8.11 (m, 2H), 7.68-7.06 (m, 7H), 6.07 (dd, *J* = 7.7, 5.1 Hz, 1H), 3.60 (dd, *J* = 10.6, 7.7 Hz, 1H), 3.57 (dd, *J* = 10.6, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.08, 164.55, 164.18, 138.29, 137.32, 132.35, 132.26, 130.11, 128.69, 128.65, 127.33, 126.18, 125.86, 115.66, 115.44, 75.54, 7.96. HRMS (ESI) *m/z* $[M - H]^+$ calcd. for $C_{15}H_{11}FIO_2^+$: 368.97932; found: 368.98123. IR ($CHCl_3$, cm^{-1}): 3019, 1709, 1214, 743.

*Compound **3c**;* White solid (351 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.70-7.64 (m, 1H), 7.47-7.23 (m, 5H), 7.08 (t, *J* = 7.7 Hz, 1H), 6.09 (dd, *J* = 7.9, 5.1 Hz, 1H), 3.62 (dd, *J* = 10.6, 8.2 Hz, 1H), 3.58 (dd, *J* = 10.6, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.83, 138.05, 137.30, 136.11, 132.58, 131.52, 130.10, 129.95, 128.78, 128.67, 128.30, 127.32, 126.21, 122.43, 75.95, 7.60. HRMS (ESI) *m/z* $[M - H]^+$ calcd. for $C_{15}H_{11}BrIO_2^+$: 428.89926; found: 428.90112. IR ($CHCl_3$, cm^{-1}): 3021, 2252, 1725, 1252, 750.

*Compound **3d**;* White solid (318 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 2.0 Hz, 1H), 7.45-7.32 (m, 6H), 6.11 (dd, *J* = 7.8, 5.2 Hz, 1H), 3.62 (dd, *J* = 10.7, 7.8 Hz, 1H), 3.58 (dd, *J* = 10.7, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.31, 138.72, 137.89, 135.25, 132.84, 131.14, 128.94, 128.77, 127.59, 127.08, 126.47, 76.68, 7.35. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{15}H_{11}Cl_2IO_2^+$: 419.91808; found: 419.92013. IR ($CHCl_3$, cm^{-1}): 2923, 1701, 1583, 1239, 697.

*Compound **3e**;* White solid (365 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.32 (m, 7H), 6.04 (dd, *J* = 7.6, 5.2 Hz, 1H), 3.93 (s, 6H), 3.92 (s, 3H), 3.63 (dd, *J* = 10.6, 7.7 Hz, 1H , 3.61 (dd, *J* = 10.6, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.91, 164.98,

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152.93, 138.49, 128.73, 126.19, 124.64, 124.06, 107.37, 107.13, 75.56, 60.91, 56.26, 8.19. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{18}H_{19}IO_5^+$: 442.02772; found: 442.02442. IR ($CHCl_3$, cm^{-1}): 2939, 1688, 1415, 1126, 763.

*Compound **3f**;* Semi solid (337 mg, 83%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.21 (m, 7H), 6.99 (dd, *J* = 10.6, 4.1 Hz, 1H), 6.92-6.86 (m, 2H), 6.00 (dd, *J* = 7.9, 5.4 Hz, 1H), 4.70 (q, *J* = 16.3 Hz, 2H), 3.49 (dd, *J* = 10.6, 7.9 Hz, 1H , 3.46 (dd, *J* = 10.6, 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.70, 157.49, 137.53, 129.41, 128.81, 128.59, 126.27, 121.61, 114.52, 75.89, 65.01, 7.08. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{16}H_{15}IO_3^+$: 382.00659; found: 382.02923. IR ($CHCl_3$, cm^{-1}): 2925, 1735, 1162, 698.

*Compound **3g**;* Semi solid (275 mg, 72%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-.29 (m, 51H), 5.85 (t, *J* = 6.5 Hz, 1H), 3.46 (d, *J* = 6.5 Hz, 2H), 2.43-2.33 (m, 1H), 2.05-1.96 (m, 1H), 1.94-1.90 (m, 1H), 1.83-1.72 (m, 2H), 1.69-1.60 (m, 1H), 1.55-1.43 (m, 2H), 1.33-1.11 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.57, 138.72, 137.42, 130.18, 128.61, 128.53, 126.17, 74.44, 43.15, 29.06, 28.83, 25.70, 25.39, 25.32, 8.12. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{15}H_{19}IO_2^+$: 358.04297; found: 358.04512. IR ($CHCl_3$, cm^{-1}): 2926, 1735, 1162, 699.

*Compound **3h**;* White solid (493 mg, 86%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.42-7.25 (m, 9H), 5.92 (dd, *J* = 7.0, 5.9 Hz, 1H), 5.30 (t, *J* = 5.9 Hz, 1H), 4.38 (d, *J* = 7.0 Hz, 2H), 4.19 (t, *J* = 6.9 Hz, 1H), 3.53-3.44 (m, 4H), 2.74-2.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.06, 156.26, 143.87, 141.28, 138.14, 128.91, 128.81, 127.65, 127.02, 126.27, 125.02, 119.95, 75.64, 66.72, 47.20, 36.53, 34.64, 7.60. MS (ESI) m/z: 542 ($[M + H]^+$, 100). IR ($CHCl_3$, cm^{-1}): 2923, 2853, 1742, 1626, 1459, 1262, 1163.

*Compound **3i**;*[26a] White solid (270 mg, 96%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (m, 2H), 7.67-7.56 (m, 2H), 7.45-7.28 (m, 9H), 5.92-5.86 (m, 1H), 5.16 (d, *J* = 7.2 Hz, 1H), 4.54-4.45 (m, 1H), 4.40 (dd, *J* = 12.4, 5.2 Hz, 2H), 4.22 (dd, *J* = 12.9, 6.6 Hz, 1H), 3.54-3.39 (m, 2H), 1.68-1.52 (m, 2H), 0.99 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 6.2 Hz, 3H), 0.96-0.81 (m, 1H). MS (ESI) m/z: 584 ($[M + H]^+$, 10), 606 ($[M + Na]^+$, 100). HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{15}H_{19}IO_2^+$: 358.04297; found: 358.04008. IR ($CHCl_3$, cm^{-1}): 2957, 1711, 1217, 736.

Representative procedure for the synthesis of 1,2-iodohydrins and iodoethers; A preformed solution of Me_3SI (237 mg, 1.16 mmol, 1.1 equiv) and $PhI(OAc)_2$ (374 mg, 1.16 mmol, 1.1 equiv) in 1 mL solvent (Method a; 1:1 acetonitrile:water, Method b; methanol) was treated with alkene **1** (**1a**, 110 mg, 100 uL, 1.05 mmol, 1.0 equiv) at room temperature. After the completion of reaction, the reaction was diluted with EtOAc (10 mL), quenched with saturated $NaHCO_3$ (5 mL), saturated aqueous sodium thiosulfate (2 mL) and extracted with EtOAc (3 X 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography to obtain the desired β-iodohydrins (**4a-4k**) or β-iodoethers (**5a-5k**).

*Compound **4a**;*[11j] Oily liquid (226 mg, 86%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 4.8 (m, 1H), 3.49 (dd, *J* = 10.3, 3.6 Hz, 1H), 3.40 (dd, *J* = 10.3, 8.8 Hz, 1H), 2.53 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.08, 128.67, 128.35, 125.71, 74.02, 15.33. HRMS (ESI) *m/z* $[M + NH_4]^+$ calcd. for $C_8H_{13}INO^+$: 266.00363; found: 266.01974. IR ($CHCl_3$, cm^{-1}): 3361, 2925, 1721, 1451, 771.

*Compound **4b**;*[11j] White solid (290 mg, 81%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.33-.29 (m, 2H), 4.80 (dd, *J* = 8.6, 3.6 Hz, 1H), 3.47 (dd, *J* = 10.4, 3.7 Hz, 1H), 3.36 (dd, *J* = 10.3, 8.7 Hz, 1H), 2.53 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.52, 134.05, 128.83, 127.12, 73.25, 15.03. HRMS (ESI) *m/z* $[M + 2H]^+$ calcd. for $C_8H_{10}ClIO^+$: 283.94539; found: 283.94752. IR ($CHCl_3$, cm^{-1}): 3357, 2926, 1492, 1370, 1229, 823.

*Compound **4c**;*[13g] Oily liquid (348 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 4.80 (d, *J* = 6.7 Hz, 1H), 3.46 (dd, *J* = 10.3, 3.6 Hz, 1H), 3.41-3.34 (m, 1H), 2.54 (s, 1H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.32, 138.08, 125.54, 125.42, 125.28, 73.88, 34.55, 31.26, 15.21. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{12}H_{18}IO^+$: 305.03968; found: 305.04122. IR ($CHCl_3$, cm^{-1}): 3352, 2959, 1510, 1410, 1214, 1084, 832, 755.

*Compound **4d**;* White solid (314 mg, 87%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.62-7.55 (m, 4H), 7.46-7.42 (m, 4H), 7.36 (t, *J* = 7.7 Hz, 1H), 4.89 (dd, *J* = 8.6, 3.1 Hz, 1H), 3.54 (dd, *J* = 10.3, 2.8 Hz, 1H), 3.44 (dd, *J* = 10.1, 8.9 Hz, 1H), 2.51 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.30, 140.54, 140.01, 128.80, 127.46, 127.42, 127.06, 126.18, 73.83, 15.30. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{14}H_{14}IO^+$: 325.00838; found: 325.011024. IR ($CHCl_3$, cm^{-1}): 3020, 2924, 2853, 1722, 1257, 742.

*Compound **4e**;* White solid (318 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85-7.71 (m 4H), 7.49-7.41 (m, 3H), 4.96 (m, 1H), 3.54 (dd, *J* = 10.3, 3.7 Hz, 1H), 3.48-3.40 (m, 1H), 2.67 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.41, 133.19, 133.16, 128.53, 128.01, 127.71, 126.38, 126.22, 124.87, 123.36, 74.09, 15.15. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{12}H_{11}IO^+$: 297.98456; found: 297.98853. IR ($CHCl_3$, cm^{-1}): 3396, 2923, 2852, 1722, 1214, 1017, 747.

*Compound **4f**;*[13e] Oily liquid (391 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.51-7.42 (m, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 3.61 (d, *J* = 7.4 Hz, 2H), 2.40 (s, 1H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.17, 128.35, 127.40, 124.66, 72.59, 28.92, 24.16. HRMS (ESI) *m/z* $[M + 2H]^+$ calcd. for $C_9H_{13}IO^+$: 263.99273; found: 263.97831. IR ($CHCl_3$, cm^{-1}): 3076, 2920, 2851, 1733, 1462, 1215, 1065, 757.

*Compound **4g**;*[13a] Oily liquid (304 mg, 90%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.7 Hz, 4H), 7.33 (d, *J* = 7.4 Hz, 3H), 7.27 (m 2H), 4.01 (s, 2H), 2.88 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

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143.35, 128.32, 127.61, 126.10, 76.58, 22.36. HRMS (ESI) *m/z* $[M + Na]^+$ calcd. for $C_{14}H_{13}INaO^+$: 346.99033; found: 346.99330. IR ($CHCl_3$, cm^{-1}): 3439, 2923, 2857, 1624, 1488, 1157, 1059, 754, 698

Compound ***4h****;*[11j] Oily liquid (371 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 1H), 7.33-7.20 (m, 3H), 5.40 (m, 1H), 4.21 (m, 1H), 3.60 (dd, *J* = 16.2, 7.3 Hz, 1H), 3.31 (dd, *J* = 16.2, 8.0 Hz, 1H), 2.37 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.05, 140.95, 128.78, 127.50, 124.31, 123.82, 85.02, 42.29, 30.08. HRMS (ESI) *m/z* $[M + 2H]^+$ calcd. for $C_9H_{11}IO^+$: 261.98436; found: 261.98706. IR ($CHCl_3$, cm^{-1}): 3015, 2922, 2852, 1735, 1214, 752.

Compound ***4i****;*[23b] Oily liquid (402 mg, 79%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.88-3.80 (m, 1H), 3.73 (s, 1H), 2.52 (d, *J* = 3.4 Hz, 1H), 2.45 (s, 1H), 2.04 (d, *J* = 6.8 Hz, 2H), 1.64-.54 (m, 2H), 1.28-1.18 (m, 1H), 1.06-0.98 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 76.58, 49.94, 44.02, 42.65, 30.27, 25.71, 24.91. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_7H_{11}IO^+$: 238.99273; found: 238.99006. IR ($CHCl_3$, cm^{-1}): 3395, 2961, 1728, 1723, 1219, 1087.

Compound ***4j****;*[13a] Oily liquid (528 mg, 77%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.04 (ddd, *J* = 12.3, 9.7, 4.3 Hz, 1H), 3.66 (m, 1H), 2.48 (ddd, *J* = 13.4, 3.9, 1.9 Hz, 1H), 2.31 (s, 1H), 2.12 (ddd, *J* = 11.3, 5.7, 3.0 Hz, 1H), 2.08-2.00 (m, 1H), 1.90-1.78 (m, 1H), 1.57-1.20 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 76.00, 43.46, 38.61, 33.65, 27.98, 24.44. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_6H_{12}IO^+$: 226.99273; found: 226.95060. IR ($CHCl_3$, cm^{-1}): 3382, 2926, 2855, 1728, 1214, 749.

Compound ***4k****;*[13f] Oily liquid (471 mg, 80%). ^1H NMR (500 MHz, $CDCl_3$) δ 4.91 (d, *J* = 7.1 Hz, 1H), 4.42 (m, 1H), 4.21 (s, 1H), 4.13-4.03 (m, 1H), 4.01 (ddd, *J* = 10.6, 7.1, 4.4 Hz, 1H), 3.72-3.56 (m, 2H), 3.46 (s, 1H), 2.47 (dd, *J* = 13.8, 3.7 Hz, 1H), 2.42-2.31 (m, 1H), 2.18-2.07 (m, 2H), 1.92-1.83 (m, 1H), 1.72-1.65 (m, 2H), 1.61 (ddd, *J* = 12.0, 9.7, 8.2 Hz, 2H), 1.34-1.21 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 98.17, 93.11, 65.39, 63.53, 36.37, 34.60, 31.34, 30.71, 27.08, 24.29. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_5H_{10}IO^+$: 228.97200; found: 228.97098. IR ($CHCl_3$, cm^{-1}): 3392, 2924, 2852, 1723, 1214, 1065, 951, 750.

Compound ***5a****;*[11j] Oily liquid (255 mg, 92%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.28 (m, 5H), 4.29 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.38-3.31 (m, 2H), 3.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.69, 128.62, 128.36, 126.48, 83.50, 57.24, 10.40. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_9H_{11}IO^+$: 261.98456; found: 261.98612. IR ($CHCl_3$, cm^{-1}): 2931, 2822, 1451, 1272, 1106, 1064, 951, 762, 697.

Compound ***5b****;*[11j] Oily liquid (321 mg, 86%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.28-7.24 (m, 2H), 4.26 (dd, *J* = 7.5, 5.1 Hz, 2H), 3.36-3.27 (m, 2H), 3.30 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.25, 134.14, 128.87, 127.92, 82.77, 57.32, 9.93. HRMS (ESI) *m/z* $[M + 2H]^+$ calcd. for $C_9H_{12}ClIO^+$: 297.96104; found: 297.95914. IR ($CHCl_3$, cm^{-1}): 2931, 2823, 1488, 1216, 1172, 1088, 823, 750, 723.

Compound ***5c****;*[11j] Oily liquid (402 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.35 (m, 2H), 7.28-7.22 (m, 2H), 4.28 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.37-3.28 (m, 2H), 3.30 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.39, 136.65, 126.16, 125.57, 83.41, 57.29, 34.61, 31.30, 10.64. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{13}H_{19}IO^+$: 318.04806; found: 318.04584. IR ($CHCl_3$, cm^{-1}): 2960, 1461, 1222, 1104, 1083, 953, 832, 735, 604.

Compound ***5d****;* Semi solid (338 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.61-7.56 (m, 4H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.38-7.30 (m, 3H), 4.33 (dd, *J* = 7.8, 5.0 Hz, 1H), 3.40-3.31 (m, 2H), 3.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.18, 140.42, 138.62, 128.70, 127.34, 127.28, 126.94, 126.87, 83.16, 57.24, 10.34. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{15}H_{15}IO^+$: 338.01676; found: 338.01513. IR ($CHCl_3$, cm^{-1}): 2927, 2821, 1485, 1221, 1102, 1079, 836, 763, 734, 696.

Compound ***5e****;* White solid (345 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.91-7.78 (m, 3H), 7.76 (s, 3H), 7.53-7.36 (m, 3H), 4.44 (dd, *J* = 7.5, 4.6 Hz, 1H), 3.48-3.35 (m, 2H), 3.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.07, 133.33, 133.12, 128.62, 127.88, 127.73, 126.33, 126.19, 126.11, 123.71, 83.66, 57.33, 10.18. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{13}H_{14}IO^+$: 313.00838; found: 313.00577. IR ($CHCl_3$, cm^{-1}): 2929, 1507, 1409, 1219, 1103, 1081, 817, 764, 663.

Compound ***5f****;*[13d] Oily liquid (458 mg, 89%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.54-7.20 (m, 5H), 3.50 (d, *J* = 10.5 Hz, 1H), 3.43 (d, *J* = 10.5 Hz, 1H), 3.13 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.25, 128.33, 127.59, 126.13, 76.77, 51.12, 23.82, 19.65. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{10}H_{14}IO^+$: 277.00838; found: 277.00658. IR ($CHCl_3$, cm^{-1}): 2926, 2853, 1486, 1214, 1039, 740.

Compound ***5g****;*[13d] White solid (332 mg, 92%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.9 Hz, 3H), 7.30 (t, *J* = 7.5 Hz, 3H), 7.27-7.21 (m, 2H), 4.12 (s, 2H), 3.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.82, 128.03, 127.26, 127.00, 80.62, 50.36, 15.84. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{15}H_{16}IO^+$: 339.02403; found: 339.02701. IR ($CHCl_3$, cm^{-1}): 2923, 2854, 1492, 1466, 1075, 698.

Compound ***5h****;*[11j] Oily liquid (371 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.1 Hz, 1H), 7.32-7.22 (m, 3H), 5.09 (d, *J* = 3.5 Hz, 1H), 4.54-.44 (m, 1H), 3.74 (dd, *J* = 17.0, 6.8 Hz, 1H), 3.58 (s, 3H), 3.29 (dd, *J* = 17.0, 4.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.34, 140.09, 129.08, 127.11, 125.15, 124.70, 93.30, 57.58, 43.50, 25.59. HRMS (ESI) *m/z* $[M + H]^+$ calcd. for $C_{10}H_{12}IO^+$: 274.99273; found: 274.99423. IR ($CHCl_3$, cm^{-1}): 2897, 1460, 1212, 1074, 743.

Compound ***5i****;*[23a] Oily liquid (421 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.72 (d, *J* = 1.0 Hz, 1H), 3.48-.38 (m, 1H), 3.30 (s, 3H), 2.61 (d, *J* = 1.6 Hz, 1H), 2.40 (m, 1H), 2.08 (dd, *J* = 11.7, 7.3 Hz, 1H), 1.82 (dd, *J* = 13.2, 7.4 Hz, 1H), 1.64-1.57 (m, 2H), 1.22 (dd, *J* = 18.8, 10.4 Hz, 1H), 0.98 (m 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 84.56, 56.11, 45.52, 43.58, 38.77, 27.67, 25.53, 25.51. HRMS

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(ESI) *m/z* [M + H]$^+$ calcd. for $C_8H_{14}IO^+$: 253.00838; found: 253.01005. IR ($CHCl_3$, cm^{-1}): 3022, 2985, 1373, 1242, 1217, 1044, 745.

Compound ***5j****;*[11j] Oily liquid (545 mg, 875%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (ddd, *J* = 10.6, 8.7, 4.2 Hz, 1H), 3.41 (s, 3H), 3.44.3.36 (m, 1H), 3.29-3.22 (m, 1H), 2.46-2.33 (m, 1H), 2.25-2.12 (m, 1H), 1.97 (dtd, *J* = 14.7, 10.9, 3.9 Hz, 1H), 1.87-1.74 (m, 1H), 1.59-1.50 (m, 1H), 1.44-1.22 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 83.86, 56.77, 37.73, 35.28, 30.22, 27.07, 23.49. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_7H_{13}IO^+$: 240.00111; found: 240.00298. IR ($CHCl_3$, cm^{-1}): 2931, 2857, 1446, 1109, 1082, 927, 752.

Compound ***5k****;*[13f] Oily liquid (509 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54 (d, *J* = 5.5 Hz, 1H), 4.07 (ddd, *J* = 8.3, 5.3, 4.5 Hz, 1H), 4.02-3.93 (m, 1H), 3.59 (ddd, *J* = 11.3, 7.7, 3.5 Hz, 1H), 3.45 (s, 3H), 2.36 (ddd, *J* = 14.6, 7.3, 3.7 Hz, 1H), 2.11-1.95 (m, 1H), 1.82-1.69 (m, 1H), 1.65-1.52 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 103.50, 63.40, 55.71, 32.72, 28.94, 25.55. HRMS (ESI) *m/z* [M + H]$^+$ calcd. for $C_6H_{12}IO^+$: 242.98765; found: 242.98498. IR ($CHCl_3$, cm^{-1}): 2922, 2852, 1461, 1214, 1037, 752.

Representative procedure for the synthesis of β-azido derivatives; Following the general procedure for β-iodo preparation using Me_3SI (237 mg, 1.16 mmol, 1.1 equiv), $PhI(OAc)_2$ (374 mg, 1.16 mmol, 1.1 equiv) and alkene (**1a,** 110 mg, 100 uL, 1.05 mmol, 1.0 equiv) and usual work, the resulting residues were treated with NaN_3 (104 mg, 1.58 mmol, 1.5 equiv) in DMF (5 mL) and stirred at 60 °C till the completion of reaction. Following the usual workup and purification by silica gel column chromatography afforded the corresponding β-azides (**6-8**) in good yields.

Compound ***6a****;*[29a] Oily liquid (189 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.29 (m, 5H), 5.92 (dd, *J* = 8.2, 3.9 Hz, 1H), 3.62 (dd, *J* = 13.1, 8.2 Hz, 1H), 3.43 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.78, 137.06, 128.68, 126.36, 74.52, 55.05, 20.98. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_{10}H_{11}N_3O_2^+$: 205.08513; found: 205.08288. IR ($CHCl_3$, cm^{-1}): 2926, 2103, 1740, 1226, 1038, 754.

Compound ***6b****;*[29a] Oily liquid (211 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.32 (m, 2H), 7.32-7.26 (m, 2H), 5.87 (dd, *J* = 7.9, 4.1 Hz, 1H), 3.60 (dd, *J* = 13.1, 7.9 Hz, 1H), 3.42 (dd, *J* = 13.1, 4.1 Hz, 1H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.65, 135.58, 134.52, 128.89, 128.79, 127.80, 73.82, 54.81, 20.90. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_{10}H_{10}ClN_3O_2^+$: 239.04623; found: 239.04453. IR ($CHCl_3$, cm^{-1}): 2924, 2101, 1743, 1223, 1040, 747.

Compound ***6c****;*[29a] Oily liquid (232 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.21 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.88 (dd, *J* = 8.2, 4.0 Hz, 1H), 3.61 (dd, *J* = 13.1, 8.2 Hz, 1H), 3.40 (dd, *J* = 13.1, 4.0 Hz, 1H), 2.34 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.78, 138.51, 134.09, 129.33, 126.34, 74.42, 54.99, 21.08, 20.98. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_{11}H_{13}N_3O_2^+$: 219.10078; found: 219.10156. IR ($CHCl_3$, cm^{-1}): 3021, 2101, 1744, 1219, 1037, 746.

Compound ***6d****;* Oily liquid (307 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.36 (m, 2H), 7.29-7.25 (m 2H), 5.91 (dd, *J* = 8.3, 3.9 Hz, 1H), 3.63 (dd, *J* = 13.1, 8.3 Hz, 1H), 3.42 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.13 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.92, 151.74, 134.02, 126.18, 125.64, 74.43, 55.06, 34.59, 31.24, 21.08. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_{14}H_{19}N_3O_2^+$: 261.14773; found: 261.14701. IR ($CHCl_3$, cm^{-1}): 2961, 2099, 1747, 1223, 1041, 830.

Compound ***6e****;* Oily liquid (153 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60-7.56 (m, 4H), 7.47-7.41 m, 4H), 7.38-7.32 (m, 1H), 5.96 (dd, *J* = 8.0, 3.8 Hz, 1H), 3.67 (dd, *J* = 13.1, 8.2 Hz, 1H), 3.47 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.87, 141.69, 140.40, 136.01, 128.91, 128.87, 128.78, 127.52, 127.46, 127.23, 127.18, 127.08, 126.87, 74.39, 55.03, 21.05. HRMS (ESI) *m/z* [M + Na]$^+$ calcd. for $C_{16}H_{15}N_3O_2Na^+$: 304.10565; found: 304.10335. IR ($CHCl_3$, cm^{-1}): 2924, 2096, 1742, 1219, 1037, 813.

Compound ***6f****;* Oily liquid (301 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 2H), 6.30 (dd, *J* = 9.8, 4.3 Hz, 1H), 3.89 (dd, *J* = 13.2, 9.8 Hz, 1H), 3.29 (dd, *J* = 13.2, 4.3 Hz, 1H), 2.43 (s, 6H), 2.24 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.81, 138.11, 136.57, 130.19, 129.79, 72.22, 52.51, 20.85, 20.76, 20.51. HRMS (ESI) *m/z* [M + H]$^+$ calcd. for $C_{13}H_{18}N_3O_2^+$: 248.13935; found: 248.13679. IR ($CHCl_3$, cm^{-1}): 2924, 2098, 1743, 1229, 1023, 852.

Compound ***6g****;*[29b] Oily liquid (273 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91-7.79 (m, 4H), 7.52-7.47 (m, 2H), 7.44 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.08 (dd, *J* = 8.2, 3.9 Hz, 1H), 3.72 (dd, *J* = 13.2, 8.2 Hz, 1H), 3.51 (dd, *J* = 13.2, 4.0 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.88, 134.41, 133.30, 133.05, 128.65, 128.02, 127.70, 126.49, 125.90, 123.75, 74.73, 55.04, 21.07. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_{14}H_{13}N_3O_2^+$: 255.10078; found: 255.09831. IR ($CHCl_3$, cm^{-1}): 3020, 2098, 1742, 1221, 1038, 745.

Compound ***7a****;*[29a] Oily liquid (56 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.29 (m, 5H), 4.88 (dd, *J* = 7.9, 4.1 Hz, 1H), 3.48 (dd, *J* = 12.6, 7.9 Hz, 1H), 3.44 (dd, *J* = 12.6, 4.1 Hz, 1H), 2.39 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.51, 128.69, 128.36, 125.88, 73.44, 58.09. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_8H_{10}N_3O^+$: 164.08184; found: 164.07989. IR ($CHCl_3$, cm^{-1}): 3432, 2923, 2853, 2100, 1258, 1062, 757, 699.

Compound ***8a****;*[29c] Oily liquid (170 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.29 (m, 5H), 4.36 (dd, *J* = 8.5, 3.6 Hz, 2H), 3.49 (dd, *J* = 13.0, 8.5 Hz, 1H), 3.31 (s, 3H), 3.21 (dd, *J* = 13.0, 3.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.37, 128.70, 128.41, 126.66, 83.16, 56.93, 56.60. HRMS (ESI) *m/z* [M]$^+$ calcd. for $C_9H_{11}N_3O^+$: 177.09021; found: 177.08798. IR ($CHCl_3$, cm^{-1}): 2922, 2853, 2101, 1218, 1120, 746.

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*Compound **8b**;*[29c] Oily liquid (224 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 2H), 7.32-7.22 (m, 2H), 4.34 (dd, *J* = 8.2, 3.7 Hz, 1H), 3.45 (dd, *J* = 13.0, 8.2 Hz, 1H), 3.30 (s, 3H), 3.19 (dd, *J* = 13.0, 3.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.08, 134.14, 128.87, 127.99, 127.89, 82.46, 56.94, 56.34. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_9H_{10}ClN_3O^+$: 211.05124; found: 211.03188. IR ($CHCl_3$, cm^{-1}): 2930, 2095, 1279, 1106, 821.

*Compound **8c**;*[29c] Oily liquid (290 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.17 (m, 5H), 4.32 (dd, *J* = 8.5, 3.6 Hz, 1H), 3.47 (dd, *J* = 13.0, 8.5 Hz, 1H), 3.29 (s, 3H), 3.18 (dd, *J* = 12.9, 3.6 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.17, 135.48, 129.35, 126.59, 82.93, 56.75, 56.58, 21.13. HRMS (ESI) *m/z* [M + Na]$^+$ calcd. for $C_{10}H_{13}N_3ONa^+$: 214.09508; found: 214.09811. IR ($CHCl_3$, cm^{-1}): 2925, 2092, 1252, 1105, 812.

*Compound **8d**;*[29c] Oily liquid (287 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.33 (m, 2H), 7.31-7.17 (m, 2H), 4.34 (dd, *J* = 8.6, 3.5 Hz, 1H), 3.48 (dd, *J* = 13.0, 8.7 Hz, 1H), 3.31 (s, 3H), 3.19 (dd, *J* = 13.0, 3.5 Hz, 1H), 1.32 (s, 10H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.37, 135.43, 126.32, 125.55, 82.93, 56.88, 56.60, 34.57, 31.30. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{13}H_{19}N_3O^+$: 219.15281; found: 219.15393. IR ($CHCl_3$, cm^{-1}): 2961, 2094, 1266, 1106, 829.

*Compound **8e**;* Oily liquid (248 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.58 (m, 4H), 7.51-7.41 (m, 2H), 7.41 -7.29 (m, 2H), 4.41 (dd, *J* = 8.5, 3.6 Hz, 1H), 3.52 (dd, *J* = 13.0, 8.5 Hz, 1H), 3.35 (s, 3H), 3.25 (dd, *J* = 13.0, 3.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.38, 140.58, 137.53, 128.79, 127.43, 127.09, 127.08, 82.92, 56.99, 56.56. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{15}H_{15}N_3O^+$: 253.12151; found: 253.12406. IR ($CHCl_3$, cm^{-1}): 2922, 2852, 2100, 1215, 749.

*Compound **8f**;*[29c] Oily liquid (230 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 1H), 4.80 (dd, *J* = 10.2, 4.0 Hz, 1H), 3.55 (t, *J* = 10.4 Hz, 1H), 3.31 (dd, *J* = 10.6, 4.0 Hz, 1H), 3.25 (s, 3H), 2.35 (s, 6H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.45, 136.65, 131.74, 130.33, 81.14, 56.87, 20.79, 20.44, 7.48. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{12}H_{17}N_3O^+$: 219.13716; found: 219.13842. IR ($CHCl_3$, cm^{-1}): 2923, 2099, 1255, 1112, 851.

*Compound **8g**;*[29c] Oily liquid (248 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.83 (m, 3H), 7.78 (s, 1H), 7.55-7.47 (m, 2H), 7.43 (dd, *J* = 8.4, 1.7 Hz, 1H), 4.52 (dd, *J* = 8.5, 3.6 Hz, 1H), 3.58 (dd, *J* = 13.0, 8.5 Hz, 1H), 3.35 (s, 3H), 3.28 (dd, *J* = 13.0, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.95, 133.36, 133.19, 128.62, 127.88, 127.73, 126.36, 126.22, 126.09, 124.00, 83.28, 56.99, 56.50. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{13}H_{13}N_3O^+$: 227.10586; found: 227.10794. IR ($CHCl_3$, cm^{-1}): 2927, 2095, 1255, 1105, 818, 744, 666.

Synthesis of benzotriazole derivative; Following the general procedure for β-iodo preparation using Me_3SI (237 mg, 1.16 mmol, 1.1 equiv), $PhI(OAc)_2$ (374 mg, 1.16 mmol, 1.1 equiv) and **1a** (110 mg, 100 uL, 1.05 mmol, 1.0 equiv) and usual work, the resulting residues were treated with 1-H-benzotriazole (152 mg, 1.27 mmol, 1.2 equiv) and DBU (320 mg/315uL, 2.1 mmol, 1.5 equiv) in DMSO (2 mL) and stirred at room temperature for 8 h. Following the usual workup and purification by silica gel column chromatography afforded **9** in 82% yield over 2 steps. Semi solid (80 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 3.0 Hz, 1H), 7.85 (d, *J* = 3.0 Hz, 1H), 7.50-7.31 (m, 7H), 6.50 (dd, *J* = 9.5, 3.9 Hz, 1H), 5.12 (dd, *J* = 13.8, 9.5 Hz, 1H), 4.97 (dd, *J* = 13.8, 3.9 Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.47, 144.51, 136.60, 128.91, 128.63, 126.58, 118.10, 74.00, 60.49, 20.84. HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{16}H_{15}N_3O_2^+$: 281.11643; found: 281.11354. IR ($CHCl_3$, cm^{-1}): 2923, 2857, 1742, 1433, 1374, 1229, 1023, 746.

Representative procedure for copper-catalyzed azide-alkyne cycloaddition; Following the general procedure for β-azido and usual work, the resulting residues were treated with phenylacetylene (130 mg/140 uL, 1.27 mmol, 1.2 equiv), CuI (400 mg, 2.1 mmol, 1.5 equiv) and *N*,*N*-diisopropylethylamine (407 mg/550 uL, 3.15 mmol, 3 equiv) in CH_3CN (2 mL) and stirred at room temperature for 3 h. Following the usual workup and purification by silica gel column chromatography afforded the triazoles **10-12** in good yields over 3 sequential steps.

*Compound **10**;* White solid (85 mg, 78%). Mp. 119-121 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.779-7.77 (m, 2H), 7.64 (s, 1H), 7.48-7.28 (m, 8H), 6.17 (dd, *J* = 7.5, 4.9 Hz, 1H), 4.78-4.68 (m, 2H), 2.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.36, 147.57, 136.18, 130.30, 128.91, 128.81, 128.72, 128.08, 126.28, 125.59, 120.25, 73.71, 54.34, 20.77. MS (ESI) m/z: 308 ([M + H]$^+$, 100), 330 ([M + Na]$^+$, 50). HRMS (ESI) *m/z* $[M]^+$ calcd. for $C_{18}H_{17}N_3O_2^+$: 307.13208; found: 307.13409. IR ($CHCl_3$, cm^{-1}): 2922, 2852, 1744, 1462, 1372, 1226, 1028, 764, 696.

*Compound **11**;*[30b] White solid (87 mg, 78%). Mp. 105-107 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.78-7.70 (m, 2H), 7.46-7.27 (m, 8H), 5.24 (dd, *J* = 8.8, 3.2 Hz, 1H), 4.65 (dd, *J* = 14.0, 3.2 Hz, 1H), 4.45 (dd, *J* = 14.0, 8.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.36, 140.14, 130.29, 128.79, 128.47, 128.10, 125.87, 125.61, 121.20, 72.88, 57.51. MS (ESI) m/z: 266 ([M + H]$^+$). IR ($CHCl_3$, cm^{-1}): 3307, 2922, 2852, 1712, 1462, 1221, 1065, 770, 693.

*Compound **12**;* White solid (92 mg, 82%). Mp. 98-100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (m, 2H), 7.83 (s, 1H), 7.49-7.29 (m, 8H), 4.68-4.55 (m, 2H), 4.50-4.40 (m, 1H), 3.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.40, 137.65, 130.70, 128.87, 128.75, 127.98, 126.60, 125.66, 121.09, 82.29, 56.96, 56.19. MS (ESI) m/z: 280 ([M + H]$^+$, 100), 302 ([M + Na]$^+$, 25). HRMS (ESI) *m/z* [M + Na]$^+$ calcd. for $C_{17}H_{17}N_3NaO^+$: 302.12638; found: 302.12898. IR ($CHCl_3$, cm^{-1}): 2923, 2852, 1726, 1461, 1217, 1107, 766, 683.

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Notes and references

1 (a) The Chemistry of Double Bonded Functional Groups; S. Patai, Ed.; Wiley: Chichester, 1997; (b) P. Phukan, P. Chakraborty and D. J. Kataki, *J. Org. Chem.,* 2006, **71**, 7533; (c) T. B. Kakule, S. Zhang, J. Zhan and E. W. Schmidt, *Org. Lett.,* 2015, **17**, 2295; (d) T. B. Kakule, Z. Lin and E. W. Schmidt, *J. Am. Chem. Soc.,* 2014, **136**, 17882.

2 For selected references, see: (a) H. Egami and M. Sodeoka, *Angew. Chem. Int. Ed.,* 2014, **53**, 8294; (b) S. R. Chemler and M. T. Bovino, *ACS Catal.,* 2013, **3**, 1076; (c) K. Muñiz and C. Martínez, *J. Org. Chem.,* 2013, **78**, 2168; (d) S.-X. Huang and K.-L. Ding, *Angew. Chem. Int. Ed.,* 2011, **50**, 7734; (e) A. Minatti and K. Muñiz, *Chem. Soc. Rev.,* 2007, **36**, 1142; (f) D. J. Chen, C. Timmons, H. X. Wei and G. G. Li, *J. Org. Chem.,* 2003, **68**, 5742.

3 Transition-metal catalyzed difunctionalization of alkenes such as dioxygenation, oxyamination, diamination, aminohalogenation, azidohydroxylation, azidocynation, oxyphopshorylation, etc have been documented. For selected examples, see; (a) X.-F. Xia, S.-L. Zhu, Z. Gu, H. Wang, W. Li, X. Liu and Y.-M. Liang, *J. Org. Chem.,* 2015, **80**, 5572; (b) G. A. Abeykoon, S. Chatterjee and J. S. Chen, *Org. Lett.,* 2014, **16**, 3248; (c) Q. Xue, J. Xie, P. Xu, K. Hu, Y. Cheng and C. Zhu, *ACS Catal.,* 2013, **3**, 1365; (d) L. Legnani and B. Morandi, *Angew. Chem., Int. Ed.,* 2016, **55**, 2248; (e) P. H. Fuller, J.-W. Kim and S. R. Chemler, *J. Am. Chem. Soc.,* 2008, **130**, 17638; (f) M. C. Paderes, J. B. Keister and S. R. Chemler, *J. Org. Chem.,* 2013, **78**, 506; (g) H. Du, W. Yuan, B. G. Zhao and Y. A. Shi, *J. Am. Chem. Soc.,* 2007, **129**, 11688; (h) P. A. Sibbald and F. E. Michael, *Org. Lett.,* 2009, **11**, 1147; (i) S. R. Chemler and M. T. Bovino, *ACS Catal*., 2013, **3**, 1076; (j) X. Ji, H. Huang, W. Wu and H. Jiang, *J. Am. Chem. Soc.,* 2013, **135**, 5286; (k) W. Wei and J. Ji, Angew. Chem., Int. Ed., 2011, **50**, 9097; (l) S.-F. Zhou, D.-P. Li, K. Liu, J.-P. Zou and O. T. J. Asekun, *Org. Chem.,* 2015, **80**, 1214; (m) L. Xu, X.-Q. Mou, Z.-M. Chen and S.-H. Wang, *Chem. Commun.,* 2014, **50**, 10676.

4 (a) E. -i. Negishi, *Angew. Chem., Int. Ed.,* 2011, **50**, 6738; (b) A. Suzuki, *Angew. Chem., Int. Ed.,* 2011, **50**, 6722; (c) C. C. C. J. Seechurn, M. O. Kitching, T. J. Colacot and V. Snieckus, *Angew. Chem., Int. Ed.,* 2012, **51**, 5062.

5 (a) D. Nair, J. Scarpello, L. White, L. Freista dos Santos, I. Vankelecom and A. Livingston, *Tetrahedron Lett.,* 2001, **42**, 8219; (b) The European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products; London, 2002; (c) J. Rivera-Utrilla, I. Bautista-Toledo, M. Ferro-Garcia, C. Moreno-Catilla, *Carbon,* 2003, **41**, 323; (d) C. Garett and K. Prasad, *Adv. Synth. Catal.,* 2004, **346**, 889.

6 For selected reviews, see: (a) P. T. Anastas, J. C. Warner, Green Chemistry: Theory and Practice; Oxford University Press: New York, 1998; (b) C.-J. Li and B. M. Trost, *Proc. Natl. Acad. Sci. U.S.A.,* 2008, **105**, 13197; (c) P. J. Dunn, *Chem. Soc. Rev.,* 2012, **41**, 1452; (d) Regulatory guidelines for metal content. Doc. Ref. CPMP/SWP/QWP/4446/00.

7 (a) J. Rodriguez and J.-P. Dulcère, *Synthesis,* 1993, 1173; (b) C. Liu, M. Zhu, W. Wei, D. Yang, H. Cui, X. Liu and H. Wang, *Org. Chem. Front.,* 2015, **2**, 1356; (c) N. O. Ilchenko, M. A. Cortés and K. J. Szabó, *ACS Catal.,* 2016, **6**, 447; (d) L. Song, S. Luo, and J.-P. Chengab, *Org. Chem. Front.,* 2016, **3**, 447, and references cited therein.

8 (a) P. Pandit, K. S. Gayen, S. Khamarui, N. Chatterjee and D. K. Maiti, *Chem. Commun.,* 2011, **47**, 6933; (b) C. Zhang, C. Tang and N. Jiao, C*hem. Soc. Rev.,* 2012, **41**, 3464; (c) K. H. Jensen, J. D. Webb and M. S. Sigman, *J. Am. Chem. Soc.,* 2010, **132**, 17471.

9 (a) H. Tera, S. Zawadzki and A. Zwierzak, *Tetrahedron*, 1981, **37**, 2675; (b) A. Klepacz and A. Zwierzak, *Tetrahedron Lett.,* 2001, **42**, 4539; (c) W. Z. Yu, F. Chen, Y. A. Cheng and Y.-Y. Yeung, *J. Org. Chem.,* 2015, **80**, 2815, and references cited therein.

10 (a) R. E. Erickson, in Marine Natural Products, ed. P. J. Scheuer, Academic Press, New York, 1986, vol. 5, p. 131; (b) P. A. Bartlett, in Asymmetric Synthesis, ed. J. D. Morrison, Academic Press, New York, 1984, vol. 3, p. 411; (b) S. D. Stamatov and J. Stawinski, *Eur. J. Org. Chem.*, 2008, 2635; (c) T. Moriuchi, M. Yamaguchi, K. Kikushima and T. Hirao, *Tetrahedron Lett.,* 2007, **48**, 15; (d) D. Urankar, I. Rutar, B. Modec and D. Dolenc, *Eur. J. Org. Chem.*, 2005, 2349.

11 (a) H. Togo and S. Iida, *Synlett*, 2006, 2159; (b) R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J. Chem. Soc. Chem. Commun.* 1973, 359; (c) R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J. Chem. Soc., Perkin Trans 1* 1974, 1858; (d) Yi Yi Myint and M. A. Pasha, *Symm. Comm.*, 2004, **34**, 4477, and refences cited therein; (e) W. R. Roush, S. Narayan, C. E. Bennett and K. Briner, *Org. Lett.,* 1999, **1**, 895; (f) R. W. Friesen and S. J. Danishefsky, *J. Am. Chem. Soc*., 1989, **111**, 6656; (g) J. Thiem, H. Karl and J. Schwentner, *Synthesis,* 1978, 696; (h) M. Adinolfi, M. Parrilli, G. Barone, G. Laonigro and L. Mangoni, *Tetrahedron Lett.,* 1976, **40**, 3661; (i) L. Mangoni, M. Adinolfi, G. Barone and M. Parrilli, *Tetrahedron Lett.* 1973, **14**, 4485; (j) M. K. Agrawal, S. Adimurthy, B. Ganguly and, P. K. Ghosh, *Tetrahedron,* 2004, **65**, 2791; (k) D. W. Gammon, H. H. Kinfe, D. E. De Vos, P. A. Jacobs and B. F. Sels, *Tetrahedron Lett.,* 2004, **45**, 9533; *J. Carbohydr. Chem.,* 2007, **26**, 141.

12 (a) Y. Guindon, B. Guérin, C. Chabot, H. Mackintosh and W. W. Olgivie, *Synlett*, 1995, 449; (b) K. Maeda, H. Shinokubo and K. Oshima, *J. Org. Chem.,* 1996, **61**, 6770.

13 (a) N. Chakraborty, S. Santra, S. K. Kundu, A. Hajra, G. V. Zyryanovbd and A. Majee, *RSC Adv.,* 2015, **5**, 56780, and references cited therein; (b) T. K. Achar, S. Maiti and P. Mal, *Org. Biomol. Chem.*, 2016, **14**, 4654; (c) N. Anand, M. Kapoor, Koul, S.; S. C. Taneja, R. L. Sharma and, G. N. Qazi *Tetrahedron Asymmetry*, 2004, **15**, 3131; (d) M. S. Yusubov, R. Y. Yusubova, V. D. Filimonov and K.-W. Chi, *Synth. Commun.* 2004, **34**, 443; (e) Rodrigo da S. Ribeiro, P. M. Esteves and M. C. S. de Mattos, *Tetrahedron Lett.* 2007, **48**, 8747; (f) B. Sels, P. Levecque, R. Brosius, D. De Vos, P. Jacobs, D. W. Gammon and H. H. Kinfe, *Adv. Synth. Catal.,* 2005, **347**, 889; (g), H. Nakayama and A. Itoh, *Tetrahedron Lett.* 2007, **48**, 1131.

14 G. K. Dewkar, S. V. Narina and A. Sudalai, *Org. Lett.,* 2003, **5**, 4501.

15 (a) M. Parrilli, G. Barone, M. Adinolfi and L. Mangoni, *Tetrahedron Lett.,* 1976, **17**, 207; (b) R. Antonioletti, M. D'Auria, A. De Mico, G. Piancatelli and A. Scettri, *Tetrahedron*, 1983, **39**, 1765**.**

16 (a) J. C. R. Bougault, *Acad. Sci.*, 1900, **130**, 1766; (b) J. C. R. Bougault, *Acad. Sci.*, 1900, **131**, 528; (c) J. Barluenga, M. A. Rodriguez, P. J. Campos and G. Asensio, *J. Chem. Soc., Chem. Commun.*, 1987, 1491.

17 (a) J. G. Smith and M. Fieser, in Fieser and Fieser's Reagent for Organic Synthesis, John Wiley and Sons, New York, vol. 1–12, 1990; (b) H. Sharghi, A. R. Massah, H. Eshghi and K. Niknam, *J. Org. Chem.,* 1998, ***63***, 1455; (c) K. Otsubo, J. Inagana and M. Yamaguchi, *Tetrahedron Lett*., 1987, ***28***, 4435; (d) P. Sarmah and N. C. Barua, *Tetrahedron Lett*., 1988,

View Article Online
DOI: 10.1039/C6OB01179A

29, 5815; (e) B. C. Ranu and S. Banerjee, *J. Org. Chem.*, 2005, **70**, 4517.
18 Weissermel, K. Industrial Organic Chemistry; Wiley-VCH: Wienheim, 1997; p. 266–267.
19 (a) J. Marco-Contelles, M. T. Molina and S. Anjum, *Chem. Rev.*, 2004, **104**, 2857.
20 (a) C. Bonini and G. Righi, *Synthesis*, 1994, 225; (b) G. Majetich, R. Hicks and S. Reister, *J. Org. Chem.*, 1997, **62**, 4321.
21 For selected references, see: (a) A. Kirschning, C. Plumeier and L. Rose, *Chem. Commun.,* 1998, 33; (b) A. Kirschning, M. A. Hashem, H. Moneneschein, L. Rose and K.-U. Schöning, *J. Org. Chem.,* 1999, **64**, 6522; (c) A.; Kirschning, M. Jesberger and A. Schönberger, *Org. Lett.,* 2001, **3**, 3623.
22 (a) T. R. Reddy, D. S. Rao, K. Babachary and S. Kashyap, *Eur. J. Org. Chem.,* 2016, 291; (b) G. Kundoor, D. S. Rao and S. Kashyap, *Asian J. Org. Chem.,* 2016, **5**, 264; (c) S. K. Battina and S. Kashyap, *Tetrahedron Lett.,* 2016, **57**, 811; (d) S. Chittela, T. R. Reddy, P. Radha Krishna and S. Kashyap, *J. Org. Chem.,* 2015, **80**, 7108; (e) T. R. Reddy, D. S. Rao and S. Kashyap, *RSC Adv.,* 2015, **5**, 28338-28343; (f) B. Srinivas, T. R. Reddy, S. Kashyap, *Carbohydr. Res.,* 2015, **406**, 86; (g) T. R. Reddy, S. Chittela and S. Kashyap, *Tetrahedron,* 2014, **70**, 9224; (h) S. Chittela, T. R. Reddy, P. Radha Krishna and S. Kashyap, *RSC Adv.,* 2014, **4**, 46327.
23 (a) J. H. Schauble, E. A. Trauffer, P. P. Deshpande and R. D. Evans, *Synthesis*, 2005, 1333; (b) R. C. Cambie, B. G. Lindsay, P. S. Rutledge and P. D. Woodgate, *J. Chem. Soc., Perkin Trans., 1* 1976, 845
24 M. F. Ruasse, G. Lo Moro, B. Galland, R. Bianchini, C. Chiappe and G. Bellucci, *J. Am. Chem. Soc.* **1997,** *119,* 12492-12502.
25 (a) N. Elming and N. Claason-Kaas, *Acta Chem. Scand.,* 1952, **6**, 535; (b) C. W. Holzapfel and D .B. G. Williams, *Tetrahedron,* 1995, **51**, 8555; (c) D. B. G. Williams and S. J. Evans, *Tetrahedron Lett.,* 2004, **45**, 7189; (d) B. M. Trost and Z. Shi, *J. Am. Chem. Soc.*, *1996*, **118**, 3037.
26 (a) A. R. Reddy, P. L. Sangwan, P. K. Chinthakindi, S. Farooq, V. Siddaiah and S. Koul, *Helv. Chim. Acta* 2013, **96**, 131; (b) C. Timchalk,*Toxicology*, 2004, **200**, 1.
27 For selected articles, see: (a) J. S. Yadav, B. V. S. Reddy, B. Jyothirmai and M. S. R. Murty, *Tetrahedron Lett.*, 2005, **46**, 6559; (b) S. Chiba, Y.-J. Xu and Y.-F. Wang, *J. Am. Chem. Soc.*, 2009, **131**, 12886; (c) C. François-Endelmond, T. Carlin, P. Thuery, O. Loreau and F. Taran, *Org. Lett.*, 2010, **12**, 40; (d) X. Sun, X. Li, S. Song, Y. Zhu, Y.-F. Liang and N. Jiao, *J. Am. Chem. Soc.* 2015, **137**, 6059.
28 (a) https://pubchem.ncbi.nlm.nih.gov/, PubChem Bioassay number AID504832; (b) S. Faizi, F. Farooqi, S. Zikr-Ur-Rehman, A. Naz, F. Noor, F. Ansari, A. Ahmad and S. A. Khan, *Tetrahedron*, 2009, **65**, 998; (c) R. I. Kureshy, A. Das, N. H. Khan, S. H. R. Abdi, S. Saravan and H. C. Bajaj, *ACS Catal.*, 2011, **1**, 1529; (d) P. J. Desjardins and R. G. Berlin, *Br. J. Clin. Pharmacol.*, 2007, **64**, 555.
29 (a) A. Kamal, A. A. Shaik, M. Sandbhor and M. S. Malik, *Tetrahedron Asymmetry*, 2004, **5**, 935; (b) L. Mesas-Sanchez, A. E. Diaz-Alvarez and P. Diner, *Tetrahedron*, 2013, **69**, 753; (c) G. Fumagalli, P. T. G. Rabet, M. F. Greaney and S. Boyd, *Angew. Chem. Int. Ed.,* 2015, **54**, 11481.
30 (a) A. Ramírez-Villalva, D. González-Calderón, C. Gonzalez-Romero, M. Morales-Rodríguez, B. Jauregui-Rodríguez, E. Cuevas-Yáñez and A. Fuentes-Benítes, *Eur. J. Med. Chem.*, 2015, **97**, 275; (b) K. Pericherla, P. Khedar, B. Khungar and A. Kumar, *Tetrahedron Lett.*, 2012, **53**, 6761; (c) S. Kim, S. -N. Cho, T. Ohc and P. Kim, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 6844.