Pergamon

SCIENCE DIRECT®

Bioorganic & Medicinal Chemistry 11 (2003) 2843–2866

BIOORGANIC & MEDICINAL CHEMISTRY

Synthesis and Structure–Antifungal Activity Relationships of 3-Aryl-5-alkyl-2,5-dihydrofuran-2-ones and Their Carbanalogues: Further Refinement of Tentative Pharmacophore Group

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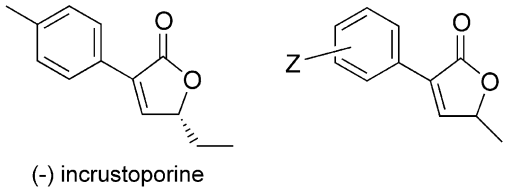
Received 13 September 2002; accepted 25 March 2003

Abstract—Two series of 3-(substituted phenyl)-5-alkyl-2,5-dihydrofuran-2-ones related to a natural product, (−)incrustoporine, were synthesized and their in vitro antifungal activity evaluated. The compounds with halogen substituents on the phenyl ring exhibited selective antifungal activity against the filamentous strains of *Absidia corymbifera* and *Aspergillus fumigatus*. On the other hand, the influence of the lenghth of the alkyl chain at C(5) was marginal. The antifungal effect of the most active compound against the above strains was higher than that of ketoconazole, and close to that of amphotericin B. In order to verify the hypothesis about a possible relationship between the Michael-accepting ability of the compounds and their antifungal activity, a series of simple carbanalogues, 2-(substituted phenyl)cyclopent-2-enones, was prepared and subjected to antifungal activity assay as well.

Introduction

The structures of biologically active natural products have often provided useful hints in the design of new pharmaceutical agents. Thus, a few years ago, we commenced a broad research programme aimed at identifying natural products with antifungal and antimycobacterial activity, and preparing their analogues with a view to developing leads to novel antifungals and antimycobacterials. Within the framework of this programme, we have published a preliminary account[1] on the relationship between structural modifications of a natural 3,5-disubstituted butenolide, (−)incrustoporine, which was originally found to possess antifungal activity against plant pathogenic fungi,[2] and in vitro activity of its synthetic derivatives (Fig. 1) against human pathogens. In particular, the activity of the most promising derivative of the first, 3-(substituted phenyl)-5-methyl-2,5-dihydrofuran-2-one series against the strain of *Absidia corymbifera* matched that of ketoconazole. We found that in order for this type of compounds to display antifungal activity, the presence of a double bond in conjugation with the carbonyl group of the γ-lactone moiety is necessary. The activity can be increased by the substitution of the phenyl ring at C(3) by halogens, while the replacement of this phenyl substituent with a five-membered heteroaryl,[3] somewhat surprisingly, reduces the antifungal effect. We have also recently shown[4] that there is probably no relationship between chirality at C(5) and the fungistatic effect, and that the introduction of an acyloxymethyl group to C(5) of the furanone ring has a positive influence.



(-) incrustoporine

Figure 1.

Based on the Michael-accepting ability of incrustoporine analogues, it appeared that they could be just a

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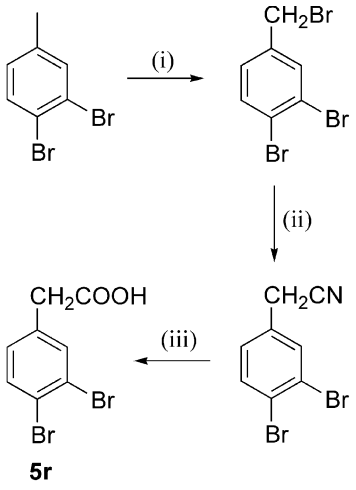
doi:10.1016/S0968-0896(03)00220-7

nonspecific class of fungal inhibitors. Nevertheless, 3-(4-nitrophenyl)-5-methyl-2,5-dihydrofuran-2-one, which is undoubtedly one of the strongest Michael acceptors of the originally reported 5-methyl series, showed virtually no activity[1] at all.

In this paper, we wish to give a full account of our studies on the 5-alkyl series, which was broadened by several new 5-methyl derivatives together with selected 5-ethyl and 5-butyl analogues. In addition, we have included some 5-alkyl compounds bearing adamantyl, naphthyl, orthocondensed and pyridyl moieties at C(3). In order to shed more light on the hypothesis between the ability of the compounds to act as Michael acceptors and their antifungal activity, a set of simple carbanalogues, 2-(substituted phenyl)cyclopent-2-enones, was prepared by Pd-mediated α-arylation of 2-iodocyclopent-2-enone, and the compounds were subjected to an antifungal activity assay. Given their structure, 2-arylcyclopent-2-enones have far greater Michael-accepting ability than the corresponding lactones, because the electron withdrawing influence of the carbonyl group is not counterbalanced by the opposite effect of the ether oxygen. Hence, if the above hypothesis is valid, the carbanalogues should exhibit higher antifungal activities.

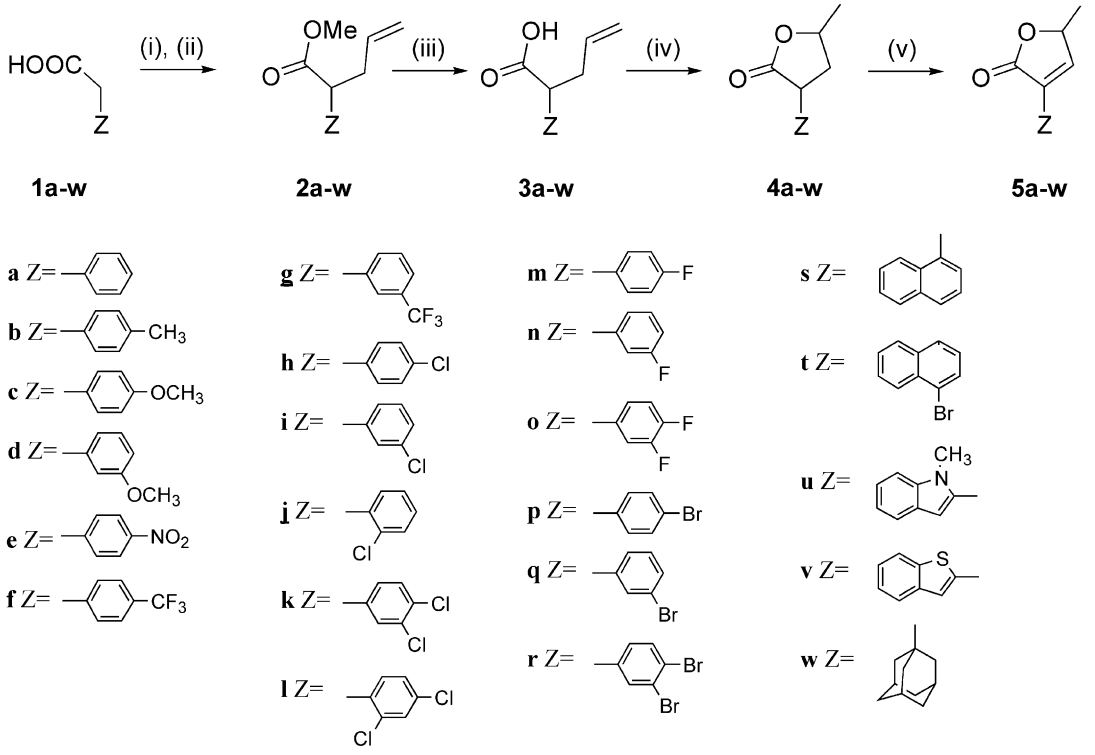


Scheme 1. (i) NBS, AIBN; (ii) KCN; (iii) LiOH, MeOH/H_2O 3:1.

Results and Discussion

Synthesis and antifungal activity of 3-(substituted phenyl)-5-methyl-2,5-dihydrofuran-2-ones

A few syntheses of 3,5-disubstituted butenolides[5,6] and 3-arylbutenolides[7] composed of several steps had been previously described. All[8,9] of the 3-(substituted phenyl)-5-methyl-2,5-dihydrofuran-2-ones **5** were prepared via a simple route described in our previous communication,[1] using commercially available substituted phenylacetic acids **1** as the starting materials; 3,4-dibromophenylacetic acid **5r** was prepared in a straightforward fashion from 3,4-dibromotoluene (Scheme 1), and 4-bromo-1-naphthylacetic acid was prepared by the bromination of 1-naphthylacetic acid.[10] The synthesis is depicted in Scheme 2. The acids were first converted into the corresponding methyl esters, and the methyl ester of 3-indolylacetic acid was also methylated on nitrogen using NaH/CH_3I. Following the deprotonation with LDA, the ester enolates were quenched with allyl bromide to afford the methyl esters



Scheme 2. (i) MeOH/$H^{\oplus}$; (ii) LDA, C_3H_5Br; (iii) LiOH; (iv) H_2SO_4 or HBr/CH_3COOH, then K_2CO_3/MeOH; (v) LDA, PhSeCl, MCPBA or H_2O_2 or $NaIO_4$.

of 2-(substituted phenyl)pent-4-enoic acids (**2**). The carboxylic group was then liberated by hydrolysis, and the resultant acids **3a**, **b**, **e**–**t**, **u**, **w** subjected to a proton-mediated cyclization onto the terminal double bond to afford 3-(substituted phenyl)-5-methyltetrahydrofuran-2-ones **4a**, **b**, **e**–**t**, **u**, **w** as mixtures of diastereomers. Following some experimentation, we found that the reaction proceeded best in concentrated H_2SO_4 at 0 °C, giving almost quantitative yield of a mixture of *trans* and *cis* isomers in the ratio of 2:1, as determined by NMR. In case of derivatives having an aryl moiety strongly susceptible to an electrophilic attack (**4c**, **4d** and **4v**), the ring closure was effected by the reaction with HBr/AcOH followed by treatment with K_2CO_3 in moist methanol. Finally, the double bond was introduced by enolization of the lactones followed by treatment with phenylselenenyl chloride, oxidation and spontaneous selenoxide elimination to yield the target compounds. For the oxidation of the intermediate phenylselanyl derivatives, H_2O_2 was sufficient in most cases. However, the target compounds bearing a strongly electron withdrawing aryl (e.g., 4-nitrophenyl) were extremely prone to a nucleophilic attack of the double bond by excess reagent and subsequent epoxide formation, and MCPBA or KIO_4 were therefore used.

The target compounds **5** and their saturated precursors **4** were evaluated for their in vitro antifungal activity on a panel of human pathogenic fungi including the representatives of both yeast and filamentous strains using the microdilution format of the NCCLS M27-A guidelines.[11] As disclosed before, saturated lactones **4** did not display any fungistatic effect; the activities of unsaturated lactones **5**, expressed as minimum inhibitory concentrations (MICs), are summarized in Table 1. In general, the compounds showed selective activity

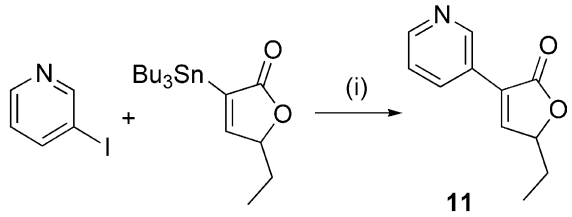
Table 1. MIC (μmol/L)[a] of compounds **5a**–**5w**

Compd	CA 24/48 h	CK 24/48 h	CT 24/48 h	CG 24/48 h	TB 24/48 h	AF 24/48 h	AC 24/48 h	TM 72/120 h
5a	>125	>125	>125	>125	>125	>125	>125	>125
	>125	>125	>125	>125	>125	>125	>125	>125
5b	>125	>125	>125	>125	>125	>125	>125	>125
	>125	>125	>125	>125	>125	>125	>125	>125
5c	>125	>125	>125	>125	>125	>125	>125	125
	>125	>125	>125	>125	>125	>125	>125	>125
5d	**62.5**	>125	>125	>125	>125	>125	125	>125
	>125	>125	>125	>125	>125	>125	>125	>125
5e	>125	>125	>125	>125	>125	>125	>125	**62.5**
	>125	>125	>125	>125	>125	>125	>125	125
5f	>125	>125	>125	>125	>125	>125	125	**62.5**
	>125	>125	>125	>125	>125	>125	125	125
5g	**15.63**	>125	>125	>125	125	125	125	**62.5**
	>125	>125	>125	>125	>125	>125	125	**62.5**
5h	**31.25**	>125	>125	>125	125	**62.5**	125	**31.25**
	>125	>125	>125	>125	>125	125	>125	**62.5**
5i	**15.63**	>125	>125	>125	125	125	>125	**31.25**
	>125	>125	>125	>125	>125	>125	>125	**62.5**
5j	>125	>125	>125	>125	>125	>125	>125	125
	>125	>125	>125	>125	>125	>125	>125	125
5k	**31.25**	>125	>125	>125	**31.25**	**7.81**	**7.81**	**31.25**
	>125	>125	>125	>125	>125	**62.5**	**31.25**	**62.5**
5l	**31.25**	>125	>125	>125	125	**62.5**	**62.5**	**31.25**
	>125	>125	>125	>125	>125	>125	**62.5**	**62.5**
5m	**62.5**	>125	>125	>125	125	125	**62.5**	>125
	>125	>125	>125	>125	>125	125	**62.5**	>125
5n	**62.5**	>125	>125	>125	>125	>125	>125	125
	>125	>125	>125	>125	>125	>125	>125	125
5o	125	>125	>125	>125	125	**62.5**	>125	**62.5**
	>125	>125	>125	>125	>125	125	>125	**62.5**
5p	**31.25**	>125	>125	>125	125	**62.5**	125	**31.25**
	62.5	>125	>125	>125	>125	>125	125	**62.5**
5q	**31.25**	>125	>125	>125	**62.5**	**62.5**	**15.63**	**62.5**
	125	>125	>125	>125	>125	>125	125	125
5r	**31.25**	>125	>125	>125	**62.5**	>125	**15.63**	**31.25**
	>125	>125	>125	>125	>125	>125	**31.25**	**62.5**
5s	**31.25**	nt	125	125	>125	125	**31.25**	**62.5**
	62.5		>125	>125	>125	>125	**31.25**	125
5t	125	>125	>125	>125	>125	**62.5**	**62.5**	**62.5**
	>125	>125	>125	>125	>125	>125	**62.5**	**62.5**
5u	>125	>125	>125	>125	>125	125	125	125
	>125	>125	>125	>125	>125	>125	>125	125
5v	>125	>125	>125	>125	>125	>125	>125	125
	>125	>125	>125	>125	>125	>125	>125	125
5w	>125	>125	>125	>125	>125	125	125	125
	>125	>125	>125	>125	>125	>125	>125	125

CA, *Candida albicans* ATCC 44859; CK, *Candida krusei* E28; CT, *Candida tropicalis* 156; CG, *Candida glabrata* 20/I; TB, *Trichosporon beigelii* 1188; AF, *Aspergillus fumigatus* 231; AC, *Absidia corymbifera* 272; TM, *Trichophyton mentagrophytes* 445.
[a]Minimum inhibitory concentration.

against filamentous strains and, even though a wider selection of substituents as compared to our initial study[1] was employed, chlorine- or bromine-substituted phenyl moiety remained the most important substituent as regards the contribution to the antifungal effect. However, it is difficult to draw a definite conclusion about the relationship between the type, position and number of halogen atoms on the phenyl ring at C(3) and the antifungal activity of the furanone derivative. The 3,4-dichlorophenyl derivative **5k** is the most effective of all chlorophenyl derivatives; the activities of the 3-chlorophenyl and 4-chlorophenyl compounds **5i** and **5h** are similar, and that of the 2-chlorophenyl derivative **5j** is practically negligible. Of the bromophenyl derivatives, 4-bromophenyl compound **5p** has also shown moderate activity against *Candida albicans*, while the 3,4-dibromophenyl derivative **5r** possessed the highest activity against *A. corymbifera*. Thus, 3-(3,4-dichlorophenyl)-5-methyl-2,5-dihydrofuran-2-one **5k** is the most active compound of the 5-methyl series.

Biological activities of the compounds are summarized in Table 2; the 3,4-dichlorophenyl derivatives **7k** and **9k** have the highest activities. As compared to the 5-methyl series, furanone **7k** with the ethyl group at C(5) is slightly more active against the filamentous strains of *A. corymbifera* (*AC*) and *Aspergillus fumigatus* (*AF*) than its 5-methyl counterpart **5k**, while the activity of the 5-butyl analogue **9k** seems to decrease. The introduction of the isosteric pyridyl moiety instead of phenyl did not bring any substantial improvement, either.



Scheme 4. $Pd_2dba_3{\cdot}CHCl_3$, $AsPh_3$, CuI, DMF.

Synthesis and antifungal activity of 3-(substituted phenyl)-5-ethyl- and 3-(substituted phenyl) -5-butyl-2,5-dihydrofuran-2-ones: comparison to standards

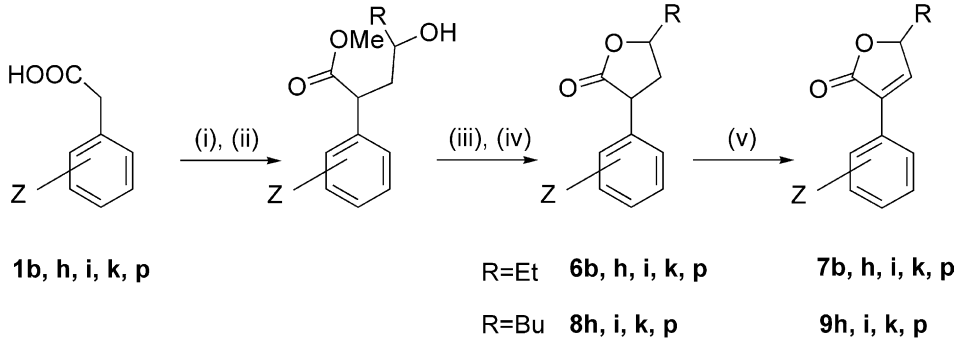
Since halogens were found to be the substituents of choice in the first round, only four 3-(substituted phenyl) compounds were synthesized in the 5-ethyl and 5-butyl series (**7** and **9**), together with 3-(4-methylphenyl)-5-ethyl-2,5-dihydrofuran-2-one (**7b**), as this compound was the racemate of incrustoporine, and the pyridyl derivative **11**. The preparation (Scheme 3) was identical to the route published[12] by Yajima and Mori for the synthesis of (−)incrustoporine, with a minor change. In the first step, these authors used 2 molar equivalents of $BF_3{\cdot}Et_2O$ per one equivalent of (2*S*)-ethyloxirane. In our hands, the reaction mixture turned into a gel, which made stirring and workup somewhat complicated. However, using just one equivalent of the Lewis acid was sufficient enough to effect the reaction. The intermediate methyl esters cyclized spontaneously on silica gel, and were therefore used without further characterization; saturated lactones **6** and **8** were obtained with yields in the range 50–70%.

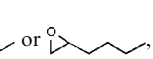
An exception was the synthesis of 3-(3-pyridyl)-5-ethyl-2,5-dihydrofuran-2-one **11**, which was prepared by the Stille-type coupling of 3-tributylstannyl-5-ethyl-2,5-dihydrofuran-2-one[3] with 3-iodopyridine (Scheme 4).

Thus, 3-(3,4-dichlorophenyl)-5-ethyl-2,5-dihydrofuran-2-one **7k** appears the most interesting derivative, the in vitro activity of which against *AF* and *AC* is somewhat better than that of ketoconazole, and not far from that of amphotericin B. The comparison of **7k** to the standards is presented in μg/mL in Table 3.

Synthesis and antifungal activity of 2-halophenylcyclopent-2-enones: refinement of the pharmacophore group

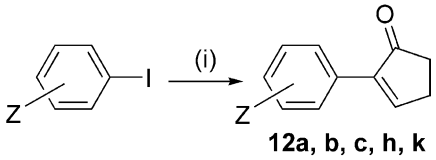
2-Arylcyclopent-2-enones, which can be considered as carbanalogues of our γ-lactones, are undoubtedly interesting compounds, given the presence of the cyclopentenone unit in a number of biologically active natural products; the screening of a recently prepared library of cross-conjugated cyclopentenones for various biological activities has also afforded useful results.[13] Since this subseries with the ether oxygen replaced by a methylene unit was structurally different, the substituents on the phenyl ring were selected according to the principles set by Toppliss.[14] Apart from 2-(3,4-dichlorophenyl)cyclopent-2-enone **12k**, all compounds had been prepared before by various procedures;[15–17] recent syntheses include the Pauson–Khand reaction[18] and [3 + 2] annulation of 3-ethoxycarbonyl-2-propenylidene(triphenyl)phosphorane with glyoxals.[19] In view of its simplicity and availability of the starting materials, a



Scheme 3. (i) MeOH/H⊕; (ii) LDA,  or , $BF_3{\cdot}Et_2O$; (iii) LiOH; (iv) H⊕; (v) LDA, PhSeCl, MCPBA.

Pd-catalyzed Negishi cross-coupling using 2-iodocyclopent-2-enone, available in a single step from cyclopent-2-enone, and organozinc reagents generated from the appropriate aryliodides, appeared as an efficient route to all derivatives of the series.

It is well known[20] that α-iodoenones undergo Pd-catalyzed reactions much less readily that their β-halogenated conterparts and, consequently, more forcing conditions must be employed in these processes. Thus, DMF was used as a solvent, and highly reactive catalysts prepared prior to the coupling by the reduction of $PdCl_2$(phosphine)$_2$ with 2 equivalents of BuLi employed. When in situ prepared $Pd(PPh_3)_2$ was used, the yield of coupling product **12a** was 25% and, surprisingly, even the more reactive $Pd[P(2\text{-furyl})_3]_2$ did not increase the yield (30%) to a significant extent in case of enone **12b**. When the combination of 2% $Pd_2(dba)_3{\cdot}CHCl_3$ and 5% of tris(2-furyl)phosphine was used as a more convenient way to generate the catalyst system,[21] the yields were also moderate to low (32% of **12h**, 16% of **12c**), with the exception of the 3,4-dichlorophenylderivative **12k**, the yield of which was 65% (Scheme 5); the yields of α-arylation using this protocol are thus strongly dependent on the substitution of the phenyl ring.



Scheme 5. BuLi, $ZnBr_2$, then Pd^0 catalyst,  .

Much to our surprise, MICs for all compounds were higher than 250 μmol/L (most of them did not display any fungistatic effect even at 1000 μmol/L!), which means that (1) Michael-accepting ability does not probably play an important role in the mechanism of antifungal action of incrustoporine derivatives and (2) the pharmacophore group can be further refined so as to include the lactone moiety (Fig. 2).

Table 2. MIC (μmol/L)[a] of compounds **7b**, **h**, **i**, **k**, **p** and **9h**, **i**, **k**, **p**

Compd	CA 24/48 h	CK 24/48 h	CT 24/48 h	CG 24/48 h	TB 24/48 h	AF 24/48 h	AC 24/48 h	TM 72/120 h
7b	>125	>125	>125	>125	>125	>125	>125	125
	>125	>125	>125	>125	>125	>125	>125	>125
7h	125	>125	>125	>125	125	**62.5**	125	**31.25**
	125	>125	>125	>125	>125	125	125	125
7i	**62.5**	>125	>125	>125	**62.5**	**62.5**	125	**62.5**
	>125	>125	>125	>125	125	>125	125	125
7k	**62.5**	>125	>125	>125	**31.25**	**7.81**	**7.81**	**7.81**
	125	>125	>125	>125	125	**15.63**	**15.63**	**31.25**
7p	**62.5**	>125	>125	>125	>125	**62.5**	**62.5**	**62.5**
	125	>125	>125	>125	>125	125	**62.5**	**125**
9h	>125	>125	>125	>125	>125	**15.63**	**15.63**	**15.63**
	>125	>125	>125	>125	>125	**15.63**	**31.25**	**31.25**
9i	>125	>125	>125	>125	125	**31.25**	**15.63**	**7.81**
	>125	>125	>125	>125	>125	**62.5**	**31.25**	**31.25**
9k	125	>125	>125	>125	**62.5**	>125	**7.81**	**7.81**
	125	>125	>125	>125	>125	>125	**31.25**	**62.5**
9p	>125	>125	>125	>125	>125	125	**31.25**	**31.25**
	>125	>125	>125	>125	>125	>125	**31.25**	**62.5**
11	**31.25**	125	125	>125	>125	>125	**31.25**	**62.5**
	62.5	125	>125	>125	>125	>125	**62.5**	**62.5**

CA, *Candida albicans* ATCC 44859; CK, *Candida krusei* E28; CT, *Candida tropicalis* 156; CG, *Candida glabrata* 20/I; TB, *Trichosporon beigelii* 1188; AF, *Aspergillus fumigatus* 231; AC, *Absidia corymbifera* 272; TM, *Trichophyton mentagrophytes* 445.
[a]Minimum inhibitory concentration.

Table 3. MIC (μg/mL)[a] of compound **7k** and ketoconazole (**KET**) and amphotericin B (**AMB**)

Compd	CA 24/48 h	CK 24/48 h	CT 24/48 h	CG 24/48 h	TB 24/48 h	AF 24/48 h	AC 24/48 h	TM 72/120 h
7k	16.1	>31.1	>31.1	>31.1	8.3	**2**	**2**	2
	31.1	>31.1	>31.1	>31.1	32.1	**4**	**4**	8.3
KET	0.06	2.08	8.31	0.13	0.06	**8.31**	**16.61**	0.52
	0.06	2.08	8.31	0.26	0.06	**8.31**	**16.61**	1.04
AMB	1	2	2	2	0.25	**0.25**	**2**	1
	1	4	2	2	0.25	**0.5**	**2**	1

CA, *Candida albicans* ATCC 44859; CK, *Candida krusei* E28; CT, *Candida tropicalis* 156; CG, *Candida glabrata* 20/I; TB, *Trichosporon beigelii* 1188; AF, *Aspergillus fumigatus* 231; AC, *Absidia corymbifera* 272; TM, *Trichophyton mentagrophytes* 445.
[a]Minimum inhibitory concentration.

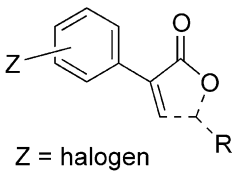


Figure 2.

Conclusion

In summary, our results have further confirmed that the substitution of the 2,5-dihydrofuranone core with a halogenated phenyl moiety at C(3) leads to selective antifungal activity against filamentous strains. The presence of chlorine in positions 3 and 4 of the phenyl ring appears to be the substitution of choice. More significantly, modifications of the substituent at C(5) based on prolonging the alkyl chain does not shift the antifungal potency to a significantly higher level. On the contrary, the activities seem to decline slightly upon replacement of ethyl with butyl. Regarding the assumptions about the pharmacophoric element, it is worthy to mention that antifungal properties are certainly not general to all butenolides; for example, protoanemonin (5-methylene-2,5-dihydrofuran-2-one) displays an antifungal effect (MIC 15 μg/mL against *C. albicans*),[22] while plakortone G [(*E*)3,5-diethyl-5-(4-ethyloct-5-enyl)-2,5-dihydrofuran-2-one] was reported[23] to possess no antifungal activity. MIC of the most active derivative against the filamentous strains *AC* and *AF* is more favourable than that of ketoconazole as the representative of azole antifungals, and close to the effect of amphotericin B. Further investigation has been directed towards the preparation of substances with more complex substituents at C(5), as some of them have been recently shown[4] to possess much more interesting in vitro antifungal activity, even though not as selective.

Experimental

General experimental procedures

THF was distilled from benzophenone ketyl; diisopropyl amine was distilled from CaH_2. The majority of the (substituted phenyl)acetic acids and (substituted phenyl)iodides were obtained from Aldrich and used as received; 3,4-dibromotoluene was purchased from Lancaster. All anhydrous reactions were performed in flame-dried Schlenk tubes under argon. Analytical thin-layer chromatography (TLC) was conducted on E. Merck TLC plates (silica gel 60 F_{254}, aluminum back). Silica gel 60 (230–400 mesh) for column chromatography was purchased from E. Merck. Melting points were determined on a Kofler block and are uncorrected. ^1H and ^{13}C NMR spectra were recorded for $CDCl_3$ solutions at ambient temperature on a Varian Mercury-Vx BB 300 spectrometer operating at 300 MHz for ^1H. Chemical shifts were recorded as δ values in parts per million (ppm), and were indirectly referenced to tetramethylsilane (TMS) via the solvent signal (7.26 for ^1H, 77.0 for ^{13}C in $CDCl_3$). All assignments were made on the basis of NOESY, gCOSY, gHSQC and gHMBC experiments. Where mixtures of diastereomers were obtained (all disubstituted tetrahydrofurans), both isomers are described separately as A and B. Infrared spectra were recorded in $CDCl_3$ on a Nicolet Impact 400 spectrophotometer. Low resolution mass spectra were measured on a Magnum Finnigan Mat apparatus. Elemental analysis was carried out on a CHNS-OCE Fisons EA 1110 instrument.

Preparation of 3,4-dibromophenylacetic acid (1r). 3,4-Dibromobenzylbromide. NBS (1.852 g, 10.37 mmol) was added to a solution of 3,4-dibromotoluene (2.592 g, 10.37 mmol) in tetrachloromethane (20 mL). The mixture was heated to 80 °C, a catalytic amount of AIBN was added and the resultant mixture was heated for 8 h. The mixture was then diluted with Et_2O, and washed successively with 5% aqueous HCl and 5% aqueous Na_2CO_3. The organic phase was dried over Na_2SO_4, and the solvent evaporated. Purification by column chromatography (petroleum ether) afforded 3,4-dibromobenzylbromide as yellow crystals in 90% yield.

Mp 41–42 °C, lit.[24] 43–44 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 d, 1H, $J = 2.2$ Hz, (Ar); 7.58 d, 1H, $J = 8.2$ Hz, (Ar); 7.19 dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 8.2$ Hz, (Ar); 4.38 s, 2H, (–CH_2); ^{13}C NMR (75 MHz,$CDCl_3$) δ 138.44, 133.91, 133.84, 128.97, 124.89, 124.69, 31.18.

3,4-Dibromophenylacetonitrile. 3,4-Dibromobenzylbromide (3.0 g, 9.12 mmol) was suspended in ethanol–water (3:1, 12 mL) and KCN (0.892 g, 13.68 mmol) was added. After heating under reflux for 10 h, the mixture was diluted with ethyl acetate, and washed with brine. The organic phase was dried over Na_2SO_4, and the solvent evaporated. Column chromatography of the crude product (petroleum ether–ethyl acetate 9:1) afforded yellow crystals in 85% yield.

Mp 65–67 °C, lit.[25] 68–69 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.64–7.59 m, 2H, (Ar); 7.15 dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 8.2$ Hz, (Ar); 3.70 s, 2H, (–CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.11, 132.93, 130.51, 127.91, 125.47, 124.63, 116.63, 22.87.

3,4-Dibromophenylacetic acid (1r). LiOH (0.954 g, 21.27 mmol) was added to a solution of 3,4-dibromophenylacetonitrile (1.950 g, 7.09 mmol) in MeOH–H_2O (3:1, 20 mL), and the reaction mixture was heated at 50 °C for 72 h. $CHCl_3$ (20 mL) was then added, and the resultant mixture was washed with 20% aqueous NaOH (40 mL). The aqueous layer was acidified with concd HCl to pH = 1, and the mixture extracted with ethyl acetate (3×). The combined extracts were dried over Na_2SO_4, and the solvent evaporated to give yellow crystals of the desired acid in 70% yield.

Mp 104–106 °C, lit.[26] 102–103 °C. ^1H NMR: (300 MHz, $CDCl_3$) δ 7.62–7.53 m, 2H, (Ar); 7.09 dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 8.2$ Hz, (Ar); 3.59 s, 2H, (–CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.61, 134.43, 133.77, 133.62, 129.55, 124.84, 123.77, 39.95.

1-(4-Bromonaphthyl)acetic acid (1t). 1-Naphtylacetic acid (5.275 g, 28.33 mmol) was dissolved in acetic acid (25 mL), bromine (1.46 mL, 28.33 mmol) was added and the mixture was heated at 80 °C for 3 h. After standing overnight, the crude product precipitated out of the solution. Recrystallization from chloroform afforded white crystals (3.320 g, 44%) of 1-(4-bromonaphthyl)-acetic acid.

Mp 173–174 °C, lit.[10] 174.5–175.5 °C. ^{1}H NMR (300 MHz, DMSO): δ 8.36–8.24 m, 1H, (Ar); 7.99–7.89 m, 1H, (Ar); 7.74 d, 1H, J = 7.7 Hz, (Ar); 7.66–7.52 m, 2H, (Ar); 7.25 d, 1H, J = 7.7 Hz, (Ar); 4.04 s, 2H, (H2). ^{13}C NMR (75 MHz, DMSO): δ 172.61, 133.45, 132.64, 131.40, 129.88, 128.97, 127.82, 127.43, 127.16, 125.19, 121.26, 38.39.

Conversion of acids 1 into the corresponding methyl esters. Acetic acids **1a–w** (12 mmol) were dissolved in methanol saturated with hydrogen chloride (100 mL) and the solution was heated under reflux for 3 h. Methanol was removed, and the residue redissolved in ethyl acetate. The solution was washed with 5 aqueous Na_2CO_3, dried over Na_2SO_4, and the solvent evaporated to give the methyl esters in quantitative yields; the compounds were used without further characterization.

Methyl 3-(*N*-methylindolyl)acetate. NaH (60 wt.%, 0.880 g, 22 mmol) in mineral oil was washed under argon with two portions of petroleum ether (2×4 mL), and suspended in dry THF (10 mL). The suspension was cooled to 0 °C, and methyl 3-indolylacetate (3.784 g, 20 mmol) in THF (15 mL) was added. After 15 min at 0 °C, methyl iodide (1.37 mL, 22 mmol) was added, and the reaction mixture stirred for 16 h at ambient temperature. The solution was then diluted with ethyl acetate (50 mL), washed with brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (petroleum ether–ethyl acetate 98:2) afforded 2.687 g (66%) of the title compound, the physical data of which were in agreement with the literature.[27]

Preparation of methyl esters of 2-substituted pent-4-enoic acids (2a–w). Butyllithium in hexanes (1.6 M, 8.27 mL) was added to a solution of diisopropylamine (1.77 mL, 12.6 mmol) in dry THF (60 mL) at 0 °C under Ar. After 10 min at 0 °C, the LDA solution was cooled to −60 °C and a solution of the methyl ester of a substituted acetic acid (**1a–w**) (12 mmol) in THF (5 mL) was added. After maintaining the mixture at −60 °C for 30 min, allyl bromide (1.09 mL, 12.6 mmol) was added dropwise. The reaction mixture was slowly allowed to warm to room temperature (2 h) in order to drive the reaction to completion. The solution was then diluted with ethyl acetate (100 mL), washed with saturated aqueous NH_4Cl, dried over Na_2SO_4, and concentrated under reduced pressure to yield the crude methyl ester of the corresponding 2-substituted pent-4-enoic acid. Purification by column chromatography (petroleum ether–ether 95:5) afforded products with yields in the range 64–96%.

Methyl 2-phenylpent-4-enoate (2a). Colorless oil, yield 70%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.35–7.23 m, 5H, (Ar); 5.81–5.67 m, 1H, (H4); 5.13–4.99 m, 2H, (H5); 3.67 dd, 1H, dd, J_1 = 6.9, J_2 = 8.5 (H2); 3.65 s, 3H, (–OCH_3); 2.91–2.80 m, 1H, (H3a); 2.59–2.48 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.70; 138.42; 135.12; 128.52; 127.78; 127.22; 116.87; 51.81; 51.24; 37.48. IR ($CDCl_3$): ν_{max} 1272, 1349, 1436, 1454, 1642, 1732, 2953, 3004, 3031 cm^{-1}. LRMS: m/z (%) 191 ($M^{\bullet+}$ + H, 8), 149 (28), 131 (100), 130 (50), 121 (61), 115 (12), 103 (6), 91 (33), 77 (13), 63 (8), 51 (12).

Methyl 2-(4-methylphenyl)pent-4-enoate (2b). Colorless oil, yield 71%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.23–7.18 m, 2H, (AA′BB′); 7.17–7.12 m, 2H, (AA′BB′); 5.80–5.66 m, 1H, (H4); 5.13–4.98 m, 2H, (H5); 3.66 s, 3H, (–OCH_3); 3.62 dd, 1H, J_1 = 7.2, J_2 = 8.5, (H2); 2.88–2.76 m, 1H, (H3a); 2.56–2.45 m, 1H, (H3b); 2.34 s, 3H, (CH_3–Ar). ^{13}C NMR (75 MHz, $CDCl_3$): 174.01; 136.95; 135.48; 135.32; 129.30; 127.72; 116.85; 51.92; 50.92; 37.53; 21.02. IR ($CDCl_3$): ν_{max} 1271, 1346, 1437, 1514, 1641, 1731, 2924, 2953, 3005 cm^{-1}. LRMS: m/z (%) 205 ($M^{\cdot++}$H, 37), 163 (48), 146 (21), 145 (100), 135 (78), 128 (15), 115 (11), 105 (10), 103 (10), 91 (9), 77 (4), 65 (4), 51 (5).

Methyl 2-(4-methoxyphenyl)pent-4-enoate (2c). Colorless oil, yield 89%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.26–7.20 m, 2H, (AA′BB′); 6.88–6.83 m, 2H, (AA′BB′); 5.79–5.64 m, 1H, (H4); 5.11–4.97 m, 2H, (H5); 3.79 s, 3H, (–OCH_3 Ar); 3.65 s, 3H, (–OCH_3); 3.60 dd, 1H, J_1 = 7.1, J_2 = 8.5, (H2); 2.86–2.73 m, 1H, (H3a); 2.55–2.43 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.93; 158.63; 135.19; 130.46; 128.79; 116.81; 113.90; 55.23; 51.96; 50.53; 37.68. IR ($CDCl_3$): ν_{max} 1438, 1512, 1584, 1611, 1641, 1731, 2838, 2954, 3004 cm^{-1}. LRMS: m/z (%) 221 ($M^{\cdot++}$H, 4), 180 (9), 179 (100), 161 (17), 151 (35), 135 (4), 115 (5), 91 (6), 77 (3), 63 (3), 51 (4).

Methyl 2-(3-methoxyphenyl)pent-4-enoate (2d). Colorless oil, yield 84%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.24 t, 1H, J = 7.9, (Ar); 6.93–6.78 m, 3H, (Ar); 5.80–5.65 m, 1H, (H4); 5.13–4.98 m, 2H, (H5); 3.80 s, 3H, (Ar–OCH_3); 3.66 s, 3H, (–OCH_3); 3.62 dd, 1H, J_1 = 7.1, J_2 = 8.8, (H2); 2.88–2.76 m, 1H, (H3a); 2.58–2.45 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.71; 159.70; 140.00; 135.19; 129.57; 120.24; 116.96; 113.58; 112.63; 55.16; 51.99; 51.34; 37.50. IR ($CDCl_3$): ν_{max} 1261, 1345, 1436, 1492, 1600, 1642, 1732, 1838, 2954, 3005 cm^{-1}. LRMS: m/z (%) 220 ($M^{\bullet+}$, 45), 205 (2), 191 (2), 179 (22), 161 (100), 151 (83), 145 (12), 134 (10), 121 (11), 108 (12), 91 (25), 77 (11), 65 (8), 51 (9).

Methyl 2-(4-nitrophenyl)pent-4-enoate (2e). Colorless oil, yield 64%. ^{1}H NMR (300 MHz, $CDCl_3$): 8.21–8.15 m, 2H, (AA′BB′); 7.51–7.45 m, 2H, (AA′BB′); 5.75–5.59 m, 1H, (H4); 5.10–4.99 m, 2H, (H5); 3.77 t, 1H, J = 7.7, (H2); 3.68 s, 3H, (–OCH_3); 2.91–2.79 m, 1H, (H3a); 2.60–2.48 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$):

172.62; 147.23; 145.64; 134.04; 129.00; 123.81; 117.93; 52.35; 51.11; 37.39. IR ($CDCl_3$): ν_{max} 1275, 1349, 1437, 1523, 1607, 1735, 2954 cm^{-1}. LRMS: *m/z* (%) 236 ($M^{\bullet+}$ + H, 13), 218 (18), 194 (5), 176 (68), 166 (39), 158 (11), 148 (19), 130 (100), 115 (25), 102 (12), 89 (17), 77 (19), 63 (17), 51 (22).

Methyl 2-(4-trifluorophenyl)pent-4-enoate (2f). Colorless oil, yield 85%. ^1H NMR (300 MHz, $CDCl_3$): 7.61–7.56 m, 2H, (AA′BB′); 7.45–7.40 m, 2H, (AA′BB′); 5.76–5.62 m, 1H, (H4); 5.12–4.99 m, 2H, (H5); 3.71 t, 1H, $J = 8.0$, (H2); 3.67 s, 3H, (–OCH_3); 2.90–2.78 m, 1H, (H3a); 2.58–2.47 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 172.97; 142.29, 142.28, 142.26 and 142.24 ($J_{C-F} = 1.4$); 134.41; 130.18, 129.75, 129.32 and 128.89 ($J_{C-F} = 32.4$); 129.37, 125.77, 122.17 and 118.56 ($J_{C-F} = 271.5$); 128.28; 125.54, 125.49, 125.44 a 125.39 ($J_{C-F} = 3.7$); 117.45; 52.21; 51.21; 37.50. LRMS: *m/z* (%) 259 ($M^{\bullet+}$ + H, 58), 239 (21), 217 (8), 199 (100), 189 (42), 177 (9), 158 (7), 141 (8), 128 (11), 109 (5), 89 (3), 73 (3), 59 (4).

Methyl 2-(3-trifluorophenyl)pent-4-enoate (2g). Colorless oil, yield 90%. ^1H NMR (300 MHz, $CDCl_3$): 7.59–7.41 m, 4H, (Ar); 5.77–5.62 m, 1H, (H4); 5.12–4.99 m, 2H, (H5); 3.71 dd, 1H, $J_1 = 7.2$, $J_2 = 8.5$, (H2); 3.68 s, 3H, (–OCH_3); 2.91–2.78 m, 1H, (H3a); 2.59–2.47 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.03; 139.25; 134.40; 131.48, 131.06, 130.63 and 130.21 ($J_{C-F} = 32.1$); 131.26, 131.25, 131.23 and 131.21 ($J_{C-F} = 1.4$); 129.30, 125.70, 122.10 and 118.50 ($J_{C-F} = 271.8$); 128.99; 124.85, 124.80, 124.75–124.70 ($J_{C-F} = 3.8$); 124.26, 124.21, 124.16–124.11 ($J_{C-F} = 3.8$); 117.50; 52.23; 51.18; 37.50. IR ($CDCl_3$): ν_{max} 1274, 1330, 1436, 1450, 1643, 1734, 2846, 2954 cm^{-1}. LRMS: *m/z* (%) 258 ($M^{\bullet+}$ + H, 5), 239 (5), 217 (6), 199 (100), 189 (38), 179 (8), 159 (11), 141 (7), 128 (6), 115 (4), 89 (2), 75 (2), 59 (4).

Methyl 2-(4-chlorophenyl)pent-4-enoate (2h). Colorless oil, yield 78%. ^1H NMR (300 MHz, $CDCl_3$): 7.31–7.27 m, 2H, (AA′BB′); 7.26–7.21 m, 2H, (AA′BB′); 5.76–5.61 m, 1H, (H4); 5.10–4.98 m, 2H, (H5); 3.66 s, 3H, (–OCH_3); 3.62 dd, 1H, $J_1 = 7.4$, $J_2 = 8.0$, (H2), 2.85–2.74 m, 1H, (H3a); 2.54–2.43 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.27; 136.75; 134.62; 133.06; 129.17; 128.63; 117.22; 52.10; 50.71; 37.52. IR ($CHCl_3$): ν_{max} 1269, 1344, 1437, 1493, 1642, 1732, 2953, 3011, 3028 cm^{-1}. LRMS: *m/z* (%) 244 ($M^{\bullet+}$, 4), 207 (1), 192 (3), 183 (68), 165 (100), 155 (93), 139 (6), 129 (32), 115 (9), 102 (10), 91 (27), 75 (13), 63 (14), 51 (16).

Methyl 2-(3-chlorophenyl)pent-4-enoate (2i). Colorless oil, yield 79%. ^1H NMR (300 MHz, $CDCl_3$): 7.32–7.30 m, 1H, (Ar); 7.26–7.16 m, 3H, (Ar); 5.77–5.62 m, 1H, (H4); 5.12–4.98 m, 2H, (H5); 3.67 s, 3H, (–OCH_3); 3.61 dd, 1H, $J_1 = 7.1$, $J_2 = 8.5$, (H2); 2.86–2.74 m. 1H, (H3a); 2.55–2.44 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.10; 140.25; 134.59; 134.30; 129.75; 128.04; 127.48; 126.07; 117.31; 52.19; 51.06; 37.50. IR ($CDCl_3$): ν_{max} 1265, 1345, 1436, 1478, 1574, 1596, 1642, 1734, 2954, 2983 cm^{-1}. LRMS: *m/z* (%) 225 ($M^{\bullet+}$, 13), 205 (1), 192 (2), 183 (14), 177 (1), 165 (100), 155 (58), 139 (4), 129 (36), 115 (8), 102 (7), 91 (16), 77 (7), 63 (8), 51 (9).

Methyl 2-(2-chlorophenyl)pent-4-enoate (2j). Colorless oil, yield 78%. ^1H NMR (300 MHz, $CDCl_3$): 7.40–7.34 m, 2H, (Ar); 7.28–7.16 m, 2H, (Ar); 5.82–5.67 m, 1H, (H4); 5.11–4.98 m, 2H, (H5); 4.25 dd, 1H, $J_1 = 7.2$, $J_2 = 8.0$, (H2); 3.68 s, 3H, (–OCH_3); 2.87–2.75 m, 1H, (H3a), 2.58–2.47 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.15; 136.23; 134.73; 133.82; 129.58; 128.68; 128.29; 126.98; 117.15; 52.16; 47.20; 36.89. IR ($CDCl_3$): ν_{max} 1267, 1348, 1436, 1476, 1642, 1733, 2953, 2982 cm^{-1}. LRMS: *m/z* (%) 225 ($M^{\bullet+}$, 36), 207 (1), 189 (22), 183 (13), 165 (100), 155 (64), 139 (4), 129 (33), 115 (8), 102 (7), 89 (12), 77 (8), 63 (7), 51 (8).

Methyl 2-(3,4-dichlorophenyl)pent-4-enoate (2k). Colorless oil, yield 85%. ^1H NMR (300 MHz, $CDCl_3$): 7.41 d overlapped, 1H, $J = 2.2$, (Ar); 7.39 d overlapped, 1H, $J = 8.3$, (Ar); 7.15 dd, 1H, $J_1 = 2.2$, $J_2 = 8.3$, (Ar); 5.75–5.59 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 3.67 s, 3H, (–OCH_3); 3.60 t, 1H, $J = 7.7$, (H2); 2.85–2.72 m, 1H, (H3a); 2.54–2.43 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 172.81; 138.39; 134.24; 132.52; 131.40; 130.42; 129.91; 127.28; 117.61; 52.29; 50.51; 37.43. IR ($CDCl_3$): ν_{max} 1284, 1344, 1437, 1474, 1562, 1643, 1735, 2852, 2929, 2954 cm^{-1}. LRMS: *m/z* (%) 258 ($M^{\bullet+}$ −H, 2), 217 (38), 199 (100), 189 (73), 173 (4), 163 (27), 136 (7), 128 (34), 111 (5), 102 (8), 89 (6), 75 (11), 59 (9), 51 (10).

Methyl 2-(2,4-dichlorophenyl)pent-4-enoate (2l). Colorless oil, yield 78%. ^1H NMR (300 MHz, $CDCl_3$): 7.40 d, 1H, $J = 2.2$, (Ar); 7.31 d, 1H, $J = 8.5$, (Ar); 7.23 dd, 1H, $J_1 = 2.2$, $J_2 = 8.5$, (Ar); 5.79–5.64 m, 1H, (H4); 5.09–4.98 m, 2H, (H5); 4.20 t, 1H, $J = 7.7$, (H2); 3.68 s, 3H, (–OCH_3); 2.85–2.72 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 172.80; 134.79; 134.54; 134.29; 133.43; 129.64; 129.34; 127.31; 117.50; 52.27; 46.70; 36.81. IR ($CDCl_3$): ν_{max} 1263, 1348, 1437,1474, 1590, 1642, 1734, 2954, 3005 cm^{-1}. LRMS: *m/z* (%) 258 ($M^{\bullet+}$ −H, 16), 241 (1), 217 (28), 199 (100), 189 (81), 163 (24), 136 (5), 128 (30), 111 (6), 101 (7), 89 (5), 75 (8), 63 (7), 51 (7).

Methyl 2-(4-fluorophenyl)pent-4-enoate (2m). Colorless oil, yield 96%. ^1H NMR (300 MHz, $CDCl_3$): 7.31–7.24 m, 2H, (AA′BB′); 7.05–6.97 m, 2H, (AA′BB′); 5.76–5.61 m, 1H, (H4); 5.10–4.97 m, 2H, (H5); 3.66 s, 3H, (–OCH_3); 3.63 dd, 1H, $J_1 = 7.2$, $J_2 = 8.3$, (H2); 2.86–2.73 m, 1H, (H3a); 2.54–2.43 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.56; 163.52 and 160.27 ($J_{C-F} = 245.1$ Hz); 134.80; 134.08 and 134.04 ($J_{C-F} = 3.4$ Hz); 129.42 and 129.31 ($J_{C-F} = 8.0$ Hz); 117.14; 115.54 and 115.25 ($J_{C-F} = 21.2$ Hz); 52.08; 50.60; 37.71. IR ($CDCl_3$): ν_{max} 1273, 1437, 1510, 1605, 1642, 1733, 2926, 2954 cm^{-1}. LRMS: *m/z* (%) 209 ($M^{\bullet+}$ + H,

17), 167 (38), 149 (100), 139 (78), 133 (8), 109 (37), 101 (4), 83 (3), 75 (4), 63 (3), 57 (4), 51 (4).

Methyl 2-(3-fluorophenyl)pent-4-enoate (2n). Colorless oil, yield 95%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.35–7.20 m, 1H, (Ar); 7.15–6.90 m, 3H, (Ar); 5.80–5.60 m, 1H, (H4); 5.15–4.95 m, 2H, (H5); 3.66 s, 3H, (–OCH_3); 3.64 dd, 1H, $J_1 = 7.4$, $J_2 = 8.0$, (H2); 2.90–2.70 m, 1H, (H3a); 2.60–2.40 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.14; 164.31 and 161.05 ($J_{C-F} = 245.6$ Hz); 140.75 a 140.66 ($J_{C-F} = 7.5$ Hz); 134.63; 129.98 and 129.87 ($J_{C-F} = 8.3$ Hz); 123.61 and 123.57 ($J_{C-F} = 2.9$ Hz); 117.4; 114.98 and 114.69 ($J_{C-F} = 21.8$ Hz); 114.36 and 114.08 ($J_{C-F} = 21.2$ Hz); 52.15; 51.10 and 51.08 ($J_{C-F} = 1.4$ Hz); 37.52. IR ($CDCl_3$): ν_{max} 1263, 1436, 1449, 1489, 1591, 1615, 1642, 1734, 2845, 2954 cm^{-1}. LRMS: m/z (%) 209 ($M^{\bullet+}$ + H, 23), 167 (10), 149 (100), 148 (71), 139 (50), 133 (10), 128 (6), 109 (38), 101 (5), 83 (4), 75 (5), 59 (4), 51 (5).

Methyl 2-(3,4-difluorophenyl)pent-4-enoate (2o). Colorless oil, yield 90%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.19–6.98 m, 3H, (Ar); 5.75–5.60 m, 1H, (H4); 5.10–4.99 m, 2H, (H5); 3.67 s, 3H, (–OCH_3); 3.60 bt, 1H, $J = 7.7$, (H2); 2.84–2.71 m, 1H, (H3a); 2.54–2.42 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.25; 151.98, 151.81, 148.68 and 148.51 ($J_{C-F} = 248.4$ and 12.7 Hz); 151.37, 151.20, 148.09 and 147.92 ($J_{C-F} = 247.8$ and 12.7 Hz); 135.34, 135.29, 135.27 and 135.21 ($J_{C-F} = 4.0$ and 5.7 Hz); 134.46; 124.13, 124.08, 124.04 and 124.00 ($J_{C-F} = 3.7$ and 6.3 Hz); 117.57; 117.38 and 117.15 ($J_{C-F} = 17.2$ Hz); 117.03 and 116.79 ($J_{C-F} = 17.8$ Hz); 52.18; 50.47; 37.53. IR ($CDCl_3$): ν_{max} 1283, 1345, 1436, 1519, 1610, 1735, 2954 cm^{-1}. LRMS: m/z (%) 227 ($M^{\bullet+}$ + H, 77), 185 (8), 167 (100), 157 (73), 127 (18), 115 (4), 101 (3), 81 (2), 63 (4).

Methyl 2-(4-bromophenyl)pent-4-enoate (2p). Colorless oil, yield 87%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.48–7.42 m, 2H, (AA′BB′); 7.22–7.16 m, 2H, (AA′BB′); 5.76–5.61 m, 1H, (H4); 5.10–4.98 m, 2H, (H5); 3.66 s, 3H, (–OCH_3); 3.61 t, 1H, $J = 7.7$, (H2); 2.86–2.73 m, 1H, (H3a); 2.55–2.42 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.21; 137.29; 134.61; 131.61; 129.57; 121.23; 117.27; 52.15; 50.81; 37.48. IR ($CDCl_3$): ν_{max} 1267, 1344, 1437, 1489, 1642, 1732, 2954, 3004 cm^{-1}. LRMS: m/z (%) 269 ($M^{\bullet+}$, 7), 251 (1), 227 (38), 209 (100), 199 (39), 183 (5), 169 (10), 148 (62), 129 (46), 115 (14), 102 (11), 89 (19), 77 (8), 63 (12), 51 (11).

Methyl 2-(3-bromophenyl)pent-4-enoate (2q). Colorless oil, yield 75%. ^{1}H NMR (300 MHz, $CDCl_3$): 7.48–7.37 m, 2H, (Ar); 7.27–7.16 m, 2H, (Ar); 5.76–5.61 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 3.67 s, 3H, (–OCH_3); 3.60 dd, 1H, $J_1 = 7.2$, $J_2 = 8.5$, (H2); 2.86–2.74 m, 1H, (H3a); 2.55–2.43 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): 173.07; 140.53; 134.56; 130.92; 130.40; 130.05; 126.51; 122.54; 117.33; 52.20; 51.03; 37.52. IR ($CDCl_3$): ν_{max} 1265, 1344, 1437, 1475, 1570, 1733, 2954, 3006 cm^{-1}. LRMS: m/z (%) 269 ($M^{\bullet+}$, 12), 251 (1), 239 (2), 227 (4), 208 (100), 199 (26), 169 (6), 157 (3), 148 (44), 129 (58), 115 (15), 102 (10), 89 (17), 77 (7), 63 (11), 51 (8).

Methyl 2-(3,4-dibromophenyl)pent-4-enoate (2r). Colorless oil, yield 75%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 d overlapped, 1H, $J = 2.2$, (Ar); 7.56 d overlapped, 1H, $J = 8.2$, (Ar); 7.12 dd, 1H, $J_1 = 2.2$, $J_2 = 8.2$, (Ar); 5.74–5.59 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 3.67 s, 3H, (–OCH_3); 3.58 t, 1H, $J = 7.7$, (H2); 2.84–2.72 m, 1H, (H3a); 2.54–2.42 m, 1H, (H3b). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.72; 139.18; 134.21; 133.61; 133.10; 128.09; 124.85; 123.57; 117.61; 52.29; 50.45; 37.37. IR ($CDCl_3$): ν_{max} 1261, 1343, 1437, 1464, 1556, 1643, 1735, 2926, 2954 cm^{-1}. LRMS: m/z (%) 349 ($M^{\bullet+}$ + H, 5), 329 (2), 307 (25), 289 (100), 279 (37), 263 (4), 249 (6), 226 (29), 208 (27), 183 (3), 169 (10), 155 (3), 128 (90), 102 (18), 91 (13), 75 (12), 63 (11), 51 (12).

Methyl 2-(1-naphthyl)-pent-4-enoate (2s). Colorless oil,[28] yield 89%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 bd, 1H, $J = 8.2$ Hz, (Ar); 7.90–7.85 m, 1H, (Ar); 7.79 bd, 1H, $J = 7.7$ Hz, (Ar); 7.60–7.42 m, 4H, (Ar); 5.90–5.74 m, 1H, (H4); 5.17–4.99 m, 2H, (H5); 4.52–4.45 m, 1H, (H2); 3.65 s, 3H, (–CH_3); 3.08–2.95 m, 1H, (H3A); 2.72–2.61 m, 1H, (H3B). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.16, 135.50, 134.76, 133.96, 131.43, 129.00, 127.89, 126.40, 125.65, 125.51, 124.89, 123.02, 116.96, 52.10, 46.56, 37.24. IR ($CDCl_3$): ν_{max} 2953, 1732, 1642, 1598, 1512, 1436, 1338 cm^{-1}. LRMS: 240 ($M^{\bullet+}$, 62), 208 (3), 199 (100), 181 (68), 171 (63), 165 (25), 152 (12), 139 (14), 128 (17), 115 (8), 102 (2), 89 (3), 77 (4), 63 (5), 51 (5).

Methyl 2-(4-bromo-1-naphthyl)-pent-4-enoate (2t). Colorless oil, yield 96%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36–8.28 m, 1H, (Ar); 8.17–8.10 m, 1H, (Ar); 7.77 d, 1H, $J = 7.8$ Hz, (Ar); 7.66–7.57 m, 2H, (Ar); 7.36 d, 1H, $J = 7.8$ Hz, (Ar); 5.89–5.70 m, 1H, (H4); 5.19–4.97 m, 2H, (H5); 4.45 dd, 1H, $J_1 = 8.5$ Hz, $J_2 = 6.3$ Hz, (H2); 3.65 s, 3H, (–CH_3); 3.09–2.92 m, 1H, (H3A); 2.73–2.57 m, 1H, (H3B). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.72, 135.08, 134.83, 132.71, 132.20, 129.63, 128.20, 127.23, 127.10, 125.44, 123.47, 122.63, 117.27, 52.21, 46.45, 37.06. IR ($CDCl_3$): ν_{max} 3082, 2953, 1732, 1642, 1509, 1436, 1380 cm^{-1}. LRMS: 318 ($M^{\bullet+}$ −H, 31), 279 (100), 261 (50), 249 (13), 235 (5), 198 (70), 179 (36), 165 (27), 152 (20), 139 (33), 126 (13), 113 (4), 100 (3), 89 (7), 76 (8), 63 (10), 50 (8).

Methyl 2-[3-(N-methylindolyl)]-pent-4-enoate (2u). Colorless crystals, yield 91%. Mp 48–50 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73–7.68 m, 1H, m, (Ar); 7.33–7.22 m, 2H, (Ar); 7.18–7.12 m, 1H, (Ar); 7.04 s, 1H, (Ar2); 5.92–5.76 m, 1H, (H4); 5.19–5.01 m, 2H, (H5); 3.99 dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 6.6$ Hz, (H2); 3.77 s, 3H, (N–CH_3); 3.68 s, 3H, (–CH_3); 2.98–2.84 m, 1H, (H3A); 2.75–2.61 m, 1H, (H3B). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.52, 136.83, 135.75, 126.88, 126.73, 121.73, 119.18, 119.14, 116.68, 111.82, 109.28, 51.85, 42.68, 37.06,

32.73. IR ($CDCl_3$): ν_{max} 2952, 2916, 1731, 1641, 1474, 1437, 1332 cm^{-1}. LRMS: 243 ($M^{\bullet+}$, 15), 202 (100), 184 (8), 174 (17), 168 (5), 158 (6), 144 (6), 130 (3), 115 (5), 102 (3), 89 (3), 77 (3), 59 (3), 51 (3).

Methyl 2-(3-benzo[b]thienyl)-pent-4-enoate (2v). Colorless oil, yield 76%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.90–7.82 m, 2H, m, (Ar5,7); 7.45–7.33 m, 3H, (Ar2,4,6); 5.89–5.73 m, 1H, (H4), 5.20–5.02 m, 2H, (H5); 4.12 dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 6.6$ Hz, (H2); 3.68 s, 3H, (–CH_3); 3.01–2.86 m, 1H, (H3A); 2.77–2.62 m, 1H, (H3B). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.21, 140.27, 138.00, 134.99, 132.80, 124.43, 124.16, 123.32, 122.88, 121.65, 117.29, 52.11, 44.90, 36.62. IR ($CDCl_3$): ν_{max} 3080, 2953, 1733, 1642, 1436, 1428, 1279 cm^{-1}. LRMS: 246 ($M^{\bullet+}$, 100), 231 (2), 205 (45), 187 (60), 177 (44), 171 (11), 161 (5), 147 (7), 115 (6), 102 (4), 89 (4), 63 (3).

Methyl 2-(1-adamantyl)-pent-4-enoate (2w). Colorless oil, yield 94%. ^1H NMR (300 MHz, $CDCl_3$): δ 5.77–5.60 m, 1H, (H4); 5.03 dq, 1H, $J_1 = 17.0$ Hz, $J_2 = 3.0$ Hz, (H5A); 4.99–4.93 m, 1H, (H5B); 3.63 s, 3H, (–CH_3), 2.40–2.19 m, 2H, (H3), 2.10 dd, 1H, $J_1 = 11.7$ Hz, $J_2 = 3.4$ Hz, (H2); 2.02–1.93 m, 3H, (CH); 1.79–1.39 m, 12H, (CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.72, 136.55, 116.20, 57.20, 50.81, 40.01, 36.88, 34.62, 30.23, 28.55. IR ($CDCl_3$): ν_{max} 2908, 2850, 1725, 1641, 1447, 1436, 1358, 1315 cm^{-1}. LRMS: 249 ($M^{\bullet+}$ + H, 32), 206 (2), 187 (9), 147 (2), 136 (17), 135 (100), 117 (3), 107 (4), 93 (5), 79 (5), 67 (3), 53 (3).

Preparation of acids 3a–w. A methyl ester of a 2-substituted pent-4-enoic acid (**2a–w**) (8 mmol) was dissolved in a mixture of MeOH–H_2O (3:1, 40 mL), and LiOH·nH_2O (57 wt% LiOH, 0.436 g, 10.4 mmol) was added to the solution. After 20 h at ambient temperature, the reaction mixture was concentrated, diluted with water and acidified with concd HCl to pH4. The resultant mixture was extracted with ethyl acetate (3×), the combined extracts dried over Na_2SO_4, and the solvent evaporated to give the crude acid **3** in a quantitative yield.

2-Phenylpent-4-enoic acid (3a). White crystals, mp 31–33 °C, lit.[29] 34 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.20–7.10 m, 5H, (Ar); 5.66–5.50 m, 1H, (H4); 4.98–4.83 m, 2H, (H5); 3.41 t, 1H, $J = 7.8$, (H2); 2.70–2.58 m, 1H, (H3a); 2.45–2.33 m, 1H, (H3b).

2-(4-Methylphenyl)pent-4-enoic acid (3b). White crystals, mp 39–41 °C, lit.[30] 91–92 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.23–7.19 m, 2H, (AA′BB′); 7.16–7.11 m, 2H, (AA′BB′); 5.79–5.65 m, 1H, (H4); 5.12–4.98 m, 2H, (H5); 3.61 t, 1H, $J = 7.8$, (H2); 2.86–2.74 m, 1H, (H3a); 2.56–2.45 m, 1H, (H3b); 2.33 s, 3H, (CH_3–Ar).

2-(4-Methoxyphenyl)pent-4-enoic acid (3c). White crystals, mp 79–81 °C, lit.[30] 81–81.5 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.27–7.21 m, 2H, (AA′BB′); 6.89–6.83 m, 2H, (AA′BB′); 5.79–5.64 m, 1H, (H4); 5.12–4.98 m, 2H, (H5); 3.79 s, 2H, (–OCH_3Ar); 3.59 t, 1H, $J = 7.7$, (H2); 2.86–2.73 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b).

2-(3-Methoxyphenyl)pent-4-enoic acid (3d). Colorless oil. ^1H NMR (300 MHz, $CDCl_3$): 7.25 t, 1H, $J = 7.8$, (Ar); 6.93–6.80 m, 3H, (Ar); 5.80–5.65 m, 1H, (H4); 5.13–4.98 m, 2H, (H5); 3.80 s, 3H, (Ar–OCH_3); 3.62 dd, 1H, $J_1 = 7.2$, $J_2 = 8.2$, (H2), 2.87–2.75 m, 1H, (H3a); 2.58–2.46 m, 1H, (H3b).

2-(4-Nitrophenyl)pent-4-enoic acid (3e). White crystals, mp 88–89 °C. ^1H NMR (300 MHz, $CDCl_3$): 8.22–8.17 m, 2H, (AA′BB′); 7.52–7.47 m, 2H, (AA′BB′); 5.75–5.59 m, 1H, (H4); 5.12–5.01 m, 2H, (H5); 3.78 t, 1H, $J = 7.7$, (H2); 2.92–2.80 m, 1H, (H3a); 2.62–2.50 m, 1H, (H3b).

2-(4-Trifluoromethylphenyl)pent-4-enoic acid (3f). Colorless oil. ^1H NMR (300 MHz, $CDCl_3$): 7.63–7.57 m, 2H, (AA′BB′); 7.48–7.42 m, 2H, (AA′BB′); 5.77–5.62 m, 1H, (H4); 5.14–5.01 m, 2H, (H5); 3.73 t, 1H, $J = 7.7$, (H2); 2.91–2.78 m, 1H, (H3a); 2.61–2.49 m, 1H, (H3b).

2-(3-Trifluoromethylphenyl)pent-4-enoic acid (3g). Colorless oil. ^1H NMR (300 MHz, $CDCl_3$): 7.60–7.42 m, 4H, (Ar); 5.78–5.63 m, 1H, (H4); 5.13–5.01 m, 2H, (H5); 3.72 t, 1H, $J = 7.7$, (H2); 2.92–2.78 m, 1H, (H3a); 2.62–2.49 m, 1H, (H3b).

2-(4-Chlorophenyl)pent-4-enoic acid (3h). Colorless oil, lit.[30] 94–95 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.33–7.28 m, 2H, (AA′BB′); 7.27–7.22 m, 2H, (AA′BB′); 5.76–5.61 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 3.62 t, 1H, $J = 7.7$, (H2); 2.85–2.74 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b).

2-(3-Chlorophenyl)pent-4-enoic acid (3i). White crystals, mp 46–48 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.33–7.31 m, 1H, (Ar); 7.28–7.18 m, 3H, (Ar); 5.77–5.62 m, 1H, (H4); 5.13–4.99 m, 2H, (H5); 3.61 t, 1H, $J = 7.7$, (H2); 2.86–2.74 m, 1H, (H3a); 2.57–2.45 m, 1H, (H3b).

2-(2-Chlorophenyl)pent-4-enoic acid (3j). Colorless oil. ^1H NMR (300 MHz, $CDCl_3$): 7.41–7.36 m, 2H, (Ar); 7.29–7.17 m, 2H, (Ar); 5.82–5.67 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 4.29 t, 1H, $J = 7.5$, (H2); 2.88–2.75 m, 1H, (H3a); 2.62–2.49 m, 1H, (H3b).

2-(3,4-Dichlorophenyl)pent-4-enoic acid (3k). White crystals, mp 53–55 °C. ^1H NMR (300 MHz, $CDCl_3$): 7.42 d overlapped, 1H, $J = 2.1$, (Ar); 7.40 d overlapped, 1H, $J = 8.4$, (Ar); 7.16 dd, 1H, $J_1 = 2.1$, $J_2 = 8.4$, (Ar); 5.75–5.59 m, 1H, (H4); 5.12–5.01 m, 2H, (H5); 3.60 t, 1H, $J = 7.7$, (H2); 2.85–2.70 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b).

2-(2,4-Dichlorophenyl)pent-4-enoic acid (3l). White crystals, mp 37–39 °C, lit.[32] 39–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.41 d, 1H, $J = 2.2$, (Ar); 7.32 d, 1H, $J = 8.5$, (Ar); 7.24 dd, 1H, $J_1 = 2.2$, $J_2 = 8.5$, (Ar); 5.79–5.64 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 4.24 t, 1H, $J = 7.7$, (H2); 2.87–2.74 m, 1H, (H3a); 2.59–2.47 m, 1H, (H3b).

2-(4-Fluorophenyl)pent-4-enoic acid (3m). White crystals, mp 68–69 °C, lit.[30] 67–69 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.32–7.24 m, 2H, (AA′BB′); 7.06–6.97 m, 2H, (AA′BB′); 5.77–5.61 m, 1H, (H4); 5.12–4.99 m, 2H, (H5); 3.63 t, 1H, $J = 7.8$, (H2); 2.86–2.72 m, 1H, (H3a); 2.57–2.42 m, 1H, (H3b).

2-(3-Fluorophenyl)pent-4-enoic acid (3n). White crystals, mp 34–36 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.35–7.20 m, 1H, (Ar); 7.15–6.90 m, 3H, (Ar); 5.80–5.60 m, 1H, (H4); 5.15–4.95 m, 2H, (H5); 3.64 t, 1H, $J = 7.7$, (H2); 2.90–2.70 m, 1H, (H3a); 2.60–2.40 m, 1H, (H3b).

2-(3,4-Difluorophenyl)pent-4-enoic acid (3o). Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): 7.21–7.00 m, 3H, (Ar); 5.76–5.60 m, 1H, (H4); 5.12–5.01 m, 2H, (H5); 3.61 t, 1H, $J = 7.7$, (H2); 2.84–2.72 m, 1H, (H3a); 2.55–2.44 m, 1H, (H3b).

2-(4-Bromophenyl)pent-4-enoic acid (3p). White crystals, mp 40–42 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.48–7.42 m, 2H, (AA′BB′); 7.22–7.16 m, 2H, (AA′BB′); 5.76–5.61 m, 1H, (H4); 5.11–4.99 m, 2H, (H5); 3.61 t, 1H, $J = 7.7$, (H2); 2.86–2.73 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b).

2-(3-Bromophenyl)pent-4-enoic acid (3q). Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): 7.49–7.39 m, 2H, (Ar); 7.28–7.16 m, 2H, (Ar); 5.77–5.62 m, 1H, (H4); 5.12–5.00 m, 2H, (H5); 3.60 t, 1H, $J = 7.7$, (H2); 2.86–2.74 m, 1H, (H3a); 2.57–2.45 m, 1H, (H3b).

2-(3,4-Dibromophenyl)pent-4-enoic acid (3r). White crystals, mp 86–88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.58 d overlapped, 1H, $J = 2.2$, (Ar); 7.57 d overlapped, 1H, $J = 8.2$, (Ar); 7.13 dd, 1H, $J_1 = 2.2$, $J_2 = 8.2$, (Ar); 5.75–5.60 m, 1H, (H4); 5.13–5.01 m, 2H, (H5); 3.59 t, 1H, $J = 7.7$, (H2); 2.85–2.73 m, 1H, (H3a); 2.56–2.44 m, 1H, (H3b).

2-(1-Naphthyl)-pent-4-enoic acid (3s). White crystals, mp 88–89 °C, lit.[31] 86–87 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (1H, bd, $J = 8.2$ Hz, Ar), 7.90–7.85 (1H, m, Ar), 7.80 (1H, bd, $J = 8.0$ Hz, Ar), 7.59–7.42 (4H, m, Ar), 5.88–5.73 (1H, m, H4), 5.17–4.99 (2H, m, H5), 4.53–4.46 (1H, m, H2), 3.07–2.94 (1H, m, H3a), 2.74–2.62 (1H, m, H3b).

2-(4-Bromo-1-naphthyl)-pent-4-enoic acid (3t). White crystals, mp 70–72 °C ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36–8.28 (1H, m, Ar), 8.16–8.09 (1H, m, Ar), 7.77 (1H, d, $J = 8.0$ Hz, Ar), 7.66–7.56 (2H, m, Ar), 7.37 (1H, d, $J = 8.0$ Hz, Ar), 5.85–5.69 (1H, m, H4), 5.18–4.99 (2H, m, H5), 4.46 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 6.7$ Hz, H2), 3.05–2.91 (1H, m, H3a), 2.73–2.60 (1H, m, H3b).

2-[3-(*N*-Methylindolyl)]-pent-4-enoic acid (3u). Colorless crystals, mp 97–99 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72–7.67 (1H, m, Ar), 7.33–7.21 (2H, m, Ar), 7.17–7.11 (1H, m, Ar), 7.04 (1H, s, Ar2), 5.91–5.75 (1H, m, H4), 5.18–4.99 (2H, m, H5), 3.97 (1H, dd, $J_1 = 8.3$ Hz, $J_2 = 7.0$ Hz, H2), 3.76 (3H, s, N–CH_3), 2.97–2.80 (1H, m, H3a), 2.75–2.59 (1H, m, H3b).

2-(3-Benzo[*b*]thienyl)-pent-4-enoic acid (3v). Colorless crystals, mp 58–60 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90–7.82 (2H, m, Ar5,7), 7.44–7.33 (3H, m, Ar2,4,6), 5.89–5.73 (1H, m, H4), 5.19–5.02 (2H, m, H5), 4.12 (1H, dd, $J_1 = 8.6$ Hz, $J_2 = 6.7$ Hz, H2), 2.99–2.87 (1H, m, H3a), 2.76–2.65 (1H, m, H3b).

2-(1-Adamantyl)pent-4-enoic acid (3w). Methyl 2-(1-adamantyl)pent-4-enoate (2.732 g, 11 mmol) was dissolved in a mixture of ethylene glycol–H_2O (3:1, 25 mL), and KOH (1.234 g, 22 mmol) was added to the solution. After heating the mixture at 210 °C for 96 h, ethylene glycol was removed by distillation, the residue was diluted with water and acidified with concd HCl to pH4. The resultant mixture was extracted with ethyl acetate (3×), the combined extracts dried over Na_2SO_4, and the solvent evaporated to afford acid **3w** as white crystals (1.389 g, 54%).

Mp 87–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.96 bs, 1H, (OH); 5.82–5.66 m, 1H, (H4); 5.07 dq, 1H, $J_1 = 17.0$ Hz, $J_2 = 3.0$ Hz, (H5A), 5.02–4.96 m, 1H, (H5B); 2.39–2.23 m, 2H, (H3); 2.09 dd, 1H, $J_1 = 10.2$ Hz, $J_2 = 4.7$ Hz, (H2); 2.03–1.93 m, 3H, (CH); 1.82–1.44 m, 12H, (CH_2).

Preparation of 3-substituted 5-methyltetrahydrofuran-2-ones 4a–b, e–t, u, w. A neat 2-substituted pent-4-enoic acid (**3a–b, e–t, u, w**) (8 mmol) was treated with concd H_2SO_4 (5 mL) at 0 °C for 20 min, and the solution was subsequently poured into brine. The mixture was neutralized with saturated aqueous Na_2CO_3 to pH8, and extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, and the solvent evaporated. The crude products were purified by column chromatography (petroleum ether–ethyl acetate 9:1) to afford the title saturated γ-lactones as mixtures of stereoisomers with yields in the range 66–100%.

3-Phenyl-5-methyltetrahydrofuran-2-one (4a). Colorless oil, yield 92%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.41–7.26 m, 5H, (Ar); 4.88–4.75 m, 1H, (H5); 3.94 dd, 1H, $J_1 = 7.2$, $J_2 = 9.3$, (H3); 2.60–2.50 m, 1H, (H4a); 2.41–2.31 m, 1H, (H4b); 1.48 d, 3H, $J = 6.3$, (–CH_3). **B**:

7.41–7.26 m, 5H, (Ar); 4.70–4.58 m, 1H, (H5); 3.90 dd, 1H, $J_1 = 8.6$, $J_2 = 12.7$, (H3); 2.84–2.73 m, 1H, (H4a); 2.10–1.97 m, 1H, (H4b); 1.51 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.14; 136.99; 128.97; 127.61; 127.56; 75.14; 45.68; 37.97; 21.04. **B**: 176.84; 136.48; 128.83; 128.07; 127.56; 74.93; 47.70; 39.79; 20.83. IR ($CDCl_3$): ν_{max} 1339, 1387, 1456, 1499, 1770, 2983 cm^{-1}. LRMS: *m*/*z* (%) 177 ($M^{\bullet+}$ + H, 48), 132 (49),131 (22), 117 (100), 115 (30), 104 (10), 103 (12), 91 (13), 77 (8), 63 (6), 51 (11).

3-(4-Methylphenyl)-5-methyltetrahydrofuran-2-one (4b). Colorless oil, yield 67%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.18–7.17 m, 4H, (Ar); 4.86–4.74 m, 1H, (H5); 3.90 dd, 1H, $J_1 = 7.2$, $J_2 = 9.3$, (H3); 2.58–2.47 m, 1H, (H4a); 2.39–2.27 m, 1H, (H4b); 2.34 s, 3H, (CH_3–Ar); 1.46 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.18–7.17 m, 4H, (Ar); 4.68–4.56 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.6$, $J_2 = 12.7$, (H3); 2.81–2.71 m, 1H, (H4a); 2.34 s, 3H, (CH_3–Ar); 2.08–1.94 m, 1H, (H4b); 1.50 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.36; 137.28; 133.94; 129.62; 127.46; 75.10; 45.29; 37.99; 21.05; 20.82. **B**: 177.08; 137.31; 133.45; 129.50; 127.91; 74.88; 47.36; 39.78; 21.05; 21.02. IR ($CDCl_3$): ν_{max} 1267, 1345, 1387, 1453, 1516, 1769, 2934, 2983 cm^{-1}. LRMS: *m*/*z* (%) 191 ($M^{\bullet+}$ + H, 100), 146 (38), 145 (21), 132 (22), 131(93), 115 (18), 103 (5), 91 (16), 77 (3), 65 (4), 51 (4).

3-(4-Nitrophenyl)-5-methyltetrahydrofuran-2-one (4e). White crystals, yield 98%. Mp 102–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 8.26–8.21 m, 2H, (AA′BB′); 7.53–7.47 m, 2H, (AA′BB′); 4.92–4.79 m, 1H, (H5); 4.10–4.03 m, 1H, (H3); 2.65–2.53 m, 1H, (H4a); 2.52–2.39 m, 1H, (H4b); 1.51 d, 3H, $J = 6.5$, (–CH_3). **B**: 8.26–8.21 m, 2H, (AA′BB′); 7.53–7.47 m, 2H, (AA′BB′); 4.76–4.63 m, 1H, (H5); 4.03 dd, 1H, $J_1 = 8.5$, $J_2 = 13.1$, (H3); 2.91–2.80 m, 1H, (H4a); 2.13–1.98 m, 1H, (H4b); 1.54 d, 3H, $J = 6.5$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 175.44; 147.12; 143.93; 128.65; 123.93; 75.15; 45.07; 37.21; 20.99. **B**: 175.16; 147.12; 143.44; 128.97; 123.79; 75.20; 47.28; 39.23; 20.71. IR (KBr pellet): ν_{max} 860, 951, 1048, 1120, 1176, 1346, 1519, 1605, 1769, 2933, 2979 cm^{-1}. LRMS: *m*/*z* (%) 222 ($M^{\bullet+}$ + H, 39), 205 (10), 191 (2), 177 (100), 160 (68), 145 (10), 131 (58), 116 (91), 103 (16), 91 (53), 77 (23), 63 (16), 51 (21).

3-(4-Trifluoromethylphenyl)-5-methyltetrahydrofuran-2-one (4f). White crystals, yield 78%. Mp 88–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.65–7.60 m, 2H, (AA′BB′); 7.45–7.40 m, 2H, (AA′BB′); 4.89–4.76 m, 1H, (H5); 4.04–3.96 m, 1H, (H3); 2.61–2.51 m, 1H, (H4a); 2.45–2.35 m, 1H, (H4b); 1.48 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.65–7.60 m, 2H, (AA′BB′); 7.45–7.40 m, 2H, (AA′BB′); 4.73–4.60 m, 1H, (H5); 3.97 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.87–2.76 m, 1H, (H4a); 2.10–1.96 m, 1H, (H4b); 1.52 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **B**: 175.95; 140.36, 140.34, 140.33 and 140.31 ($J_{C-F} = 1.4$ Hz); 130.56, 130.12, 129.69 and 129.26 ($J_{C-F} = 32.6$ Hz); 129.37, 125.76, 122.16 and 118.56 ($J_{C-F} = 272.2$ Hz); 128.50; 125.83, 125.78, 125.73 and 125.68 ($J_{C-F} = 3.8$ Hz); 75.10; 47.39; 39.46; 20.72. IR (KBr pellet): ν_{max} 1071, 1121, 1333, 1391, 1622, 1767 cm^{-1}. LRMS: *m*/*z* (%) 245 ($M^{\bullet+}$ + H, 42), 225 (13), 200 (91), 185 (90), 172 (27), 165 (60), 159 (14), 145 (15), 131 (100), 115 (16), 103 (19), 91 (13), 77 (10), 69 (13), 63 (8).

3-(3-Trifluoromethylphenyl)-5-methyltetrahydrofuran-2-one (4g). Colorless oil, yield 87%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.62–7.45 m, 4H, (Ar); 4.89–4.78 m, 1H, (H5); 4.01 dd, 1H, $J_1 = 8.3$, $J_2 = 9.2$, (H3); 2.63, 2.51 m, 1H, (H4a); 2.47–2.36 m, 1H, (H4b); 1.49 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.62–7.45 m, 4H, (Ar); 4.73–4.60 m, 1H, (H5); 3.96 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.88–2.77 m, 1H, (H4a); 2.11–1.97 m, 1H, (H4b); 1.53 d, 3H, $J = 6.0$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.06; 137.69; 131.08, 131.07, 131.05 and 131.04 ($J_{C-F} = 1.1$ Hz); 129.38; 124.50, 124.45, 124.40 and 124.36 ($J_{C-F} = 3.8$ Hz); 75.10; 45.20; 37.58; 21.07. **B**: 175.76; 137.17; 132.08, 131.65, 131.22 and 130.79 ($J_{C-F} = 32.4$ Hz); 131.48, 131.47, 131.45 and 131.43 ($J_{C-F} = 1.3$ Hz); 129.23; 129.22, 125.61, 122.01 and 118.41 ($J_{C-F} = 272.0$ Hz); 124.85, 124.80, 124.75 and 124.69 ($J_{C-F} = 3.8$ Hz); 124.52, 124.47, 124.42 and 124.36 ($J_{C-F} = 3.8$ Hz); 75.07; 47.39; 39.53; 20.81. IR ($CDCl_3$): ν_{max} 1268, 1327, 1389, 1449, 1494, 1770, 2936, 2984 cm^{-1}. LRMS: *m*/*z* (%) 245 ($M^{\bullet+}$ + H, 100), 225 (6), 200 (14), 185 (13), 172 (7), 165 (12), 151 (6), 131 (14), 115 (4), 103 (4), 91 (3), 77 (3), 51 (3).

3-(4-Chlorophenyl)-5-methyltetrahydrofuran-2-one (4h). White crystals, yield 84%. Mp 38–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.36–7.31 m, 2H, (AA′BB′); 7.26–7.20 m, 2H, (AA′BB′); 4.85–4.74 m, 1H, (H5); 3.91 dd, 1H, $J_1 = 7.7$, (H3); 2.57, 2.46 m, 1H, (H4a); 2.41–2.30 m, 1H, (H4b); 1.47 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.36–7.31 m, 2H, (AA′BB′); 7.26–7.20 m, 2H, (AA′BB′); 4.69–4.57 m, 1H, (H5); 3.87 dd, 1H, $J_1 = 8.6$, $J_2 = 13.0$, (H3); 2.83–2.72 m, 1H, (H4a); 2.06–1.91 m, 1H, (H4b); 1.50 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.64; 135.33; 133.50; 129.07; 129.02; 75.06; 44.84; 37.61; 20.96. **B**: 176.35; 134.84; 133.50; 129.41; 128.94; 74.96; 47.00; 39.54; 20.73. IR ($CHCl_3$): ν_{max} 1268, 1345, 1388, 1494, 1599, 1770, 2936, 2983, 3023 cm^{-1}. LRMS: *m*/*z* (%) 211 ($M^{\bullet+}$, 3), 166 (48), 151 (46), 138 (22), 131 (100), 115 (45), 103 (23), 91 (21), 77 (20), 63 (14), 55 (4), 51 (18).

3-(3-Chlorophenyl)-5-methyltetrahydrofuran-2-one (4i). Colorless oil, yield 94%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.31–7.26 m, 3H, (Ar); 7.22–7.15 m, 1H, (Ar); 4.87–4.75 m, 1H, (H5); 3.95–3.87 m, 1H, (H3); 2.60–2.47 m, 1H, (H4a); 2.43–2.30 m, 1H, (H4b); 1.47 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.31–7.26 m, 3H, (Ar); 7.22–7.15 m, 1H, (Ar); 4.70–4.57 m, 1H, (H5); 3.87 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.85–2.72 m, 1H, (H4a); 2.08–1.92 m, 1H, (H4b); 1.51 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.20; 138.68; 134.63; 130.09; 128.15; 127.76; 125.79; 75.13; 45.21; 37.64; 21.08. **B**:

175.89; 138.19; 134.47; 129.95; 128.15; 127.72; 126.23; 74.99; 47.26; 39.53; 20.84. IR ($CDCl_3$): ν_{max} 1346, 1388, 1480, 1575, 1599, 1774, 2983 cm^{-1}. LRMS: *m*/*z* (%) 211 ($M^{\bullet+}$, 28), 166 (48), 151 (23), 138 (12), 131 (100), 115 (32), 103 (19), 91 (15), 77 (11), 63 (8), 51 (11).

3-(2-Chlorophenyl)-5-methyltetrahydrofuran-2-one (4j). Colorless oil, yield 87%. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.43–7.37 m, 1H, (Ar); 7.31–7.21 m, 3H, (Ar); 4.85–4.74 m, 1H, (H5); 4.35–4.28 m, 1H, (H3); 2.45–2.39 m, 2H, (H4); 1.48 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.43–7.37 m, 1H, (Ar); 7.31–7.21 m, 3H, (Ar); 4.74–4.61 m, 1H, (H5); 4.31 dd, 1H, $J_1 = 8.8$, $J_2 = 12.5$, (H3); 2.90–2.79 m, 1H, (H4a); 2.05–1.88 m, 1H, (H4b); 1.51 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.37; 135.26; 133.81; 129.85; 129.65; 129.00; 127.29; 75.07; 44.06; 37.33; 21.14. **B**: 175.86; 134.69; 133.93; 129.72; 129.65; 128.88; 127.33; 75.21; 45.96; 38.95; 20.93. IR ($CDCl_3$): ν_{max} 1270, 1348, 1388, 1444, 1480, 1770, 2934, 2984 cm^{-1}. LRMS: *m*/*z* (%) 211 ($M^{\bullet+}$, 28), 195 (1), 184 (1), 175 (1), 166 (50), 151 (31), 131 (100), 115 (38), 103 (22), 91 (15), 77 (13), 63 (10), 51 (13).

3-(3,4-Dichlorophenyl)-5-methyltetrahydrofuran-2-one (4k). White crystals, quantitative yield. Mp 56–58 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.45–7.37 m, 2H, (Ar); 7.17–7.11 m, 1H, (Ar); 4.86–4.74 m, 1H, (H5); 3.93–3.86 m, 1H, (H3); 2.57–2.46 m, 1H, (H4a); 2.42–2.31 m, 1H, (H4b); 1.46 d, 3H, $J = 6.4$, (–CH_3). **B**: 7.45–7.37 m, 2H, (Ar); 7.17–7.11 m, 1H, (Ar); 4.69–4.57 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.83–2.73 m, 1H, (H4a); 2.04–1.91 m, 1H, (H4b); 1.50 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 175.82; 136.76; 132.80; 131.66; 130.69; 129.60; 127.00; 75.08; 44.48; 37.29; 21.00. **B**: 175.53; 136.30; 132.64; 131.66; 130.56; 129.94; 127.37; 75.03; 46.65; 39.26; 20.74. IR ($CHCl_3$): ν_{max} 1345, 1389, 1473, 1564, 1770, 2935, 2983, 3026 cm^{-1}. LRMS: *m*/*z* (%) 245 ($M^{\bullet+}$, 27), 200 (68), 185 (37), 165 (100), 150 (37), 137 (15), 129 (24), 115 (20), 102 (18), 87 (5), 75 (15), 63 (8), 50 (11).

3-(2,4-Dichlorophenyl)-5-methyltetrahydrofuran-2-one (4l). White crystals, yield 77%, Mp 45–47 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.43 d, 1H, $J = 2.1$, (Ar); 7.26 dd, 1H, $J_1 = 2.1$, $J_2 = 8.5$, (Ar); 7.18 d, 1H, $J = 8.5$, (Ar); 4.85–4.73 m, 1H, (H5); 4.27 t, 1H, $J = 9.0$, (H3); 2.44–2.37 m, 2H, (H4), 1.48 d, 3H, $J = 6.6$, (–CH_3). **B**: 7.42 d, 1H, $J = 2.2$, (Ar); 7.28–7.19 m, 2H, (Ar); 4.73–4.61 m, 1H, (H5); 4.26 dd, 1H, $J_1 = 8.8$, $J_2 = 12.6$, (H3); 2.89–2.78 m, 1H, (H4a); 1.97–1.82 m, 1H, (H4b); 1.50 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 175.87; 134.57; 134.06; 133.84; 129.88; 129.67; 127.59; 75.05; 43.45; 37.12; 21.13. **B**: 175.41; 134.67; 134.06; 133.27; 130.44; 129.53; 127.66; 75.26; 45.49; 38.87; 20.88. IR ($CDCl_3$): ν_{max} 1346, 1386, 1477,1560, 1591, 1773, 2934, 2982 cm^{-1}. LRMS: *m*/*z* (%) 245 ($M^{\bullet+}$, 100), 226 (1), 215 (1), 200 (50), 185 (26), 165 (72), 150 (29), 137 (12), 129 (16), 115 (15), 102 (18), 87 (4), 75 (10), 63 (6), 50 (8).

3-(4-Fluorophenyl)-5-methyltetrahydrofuran-2-one (4m). White crystals, yield 67%. Mp 33–35 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.31–7.21 m, 2H, (AA′BB′); 7.09–7.01 m, 2H, (AA′BB′); 4.86–4.74 m, 1H, (H5); 3.92 dd, 1H, $J_1 = 7.9$, (H3); 2.57–2.46 m, 1H, (H4a); 2.41–2.30 m, 1H, (H4b); 1.47 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.31–7.21 m, 2H, (AA′BB′); 7.09–7.01 m, 2H, (AA′BB′); 4.69–4.57 m, 1H, (H5); 3.88 dd, 1H, $J_1 = 8.5$, (H3), 2.83–2.73 m, 1H, (H4a); 2.05–1.92 m, 1H, (H4b); 1.49 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.69; 163.18 and 159.92 ($J_{C-F} = 245.6$ Hz); 132.51 and 132.47 ($J_{C-F} = 3.2$ Hz); 129.06 and 128.96 ($J_{C-F} = 8.0$ Hz); 115.47 and 115.18 ($J_{C-F} = 21.5$ Hz); 74.89; 44.42; 37.35; 20.64. **B**: 176.44; 163.18 and 159.92 ($J_{C-F} = 245.6$ Hz); 132.08 and 132.03 ($J_{C-F} = 3.2$ Hz); 129.45 and 129.34 ($J_{C-F} = 8.0$ Hz); 115.32 and 115.04 ($J_{C-F} = 21.5$ Hz); 74.78; 46.64; 39.40; 20.42. IR ($CDCl_3$): ν_{max} 1267, 1346, 1388, 1453, 1513, 1608, 1770, 2933, 2983 cm^{-1}. LRMS: *m*/*z* (%) 195 ($M^{\bullet+}$ + H, 21), 166 (4), 150 (45), 135 (100), 123 (13), 115 (23), 109 (18), 96 (8), 83 (5), 75 (9), 63 (5), 57 (6), 50 (6).

3-(3-Fluorophenyl)-5-methyltetrahydrofuran-2-one (4n). Colorless oil, yield 79%. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.40–7.25 m, 1H, (Ar); 7.10–6.90 m, 3H, (Ar); 4.90–4.70 m, 1H, (H5); 3.97–3.90 m, 1H, (H3); 2.60–2.45 m, 1H, (H4a); 2.45–2.30 m, 1H, (H4b); 1.47 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.40–7.25 m, 1H, (Ar); 7.10–6.90 m, 3H, (Ar); 4.70–4.55 m, 1H, (H5); 3.90 dd, 1H, $J_1 = 8.5$, $J_2 = 12.8$, (H3); 2.85–2.70 m, 1H, (H4a); 2.10–1.90 m, 1H, (H4b); 1.49 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.24; 164.41 and 161.14 ($J_{C-F} = 246.2$ Hz); 139.13 and 139.03 ($J_{C-F} = 7.7$ Hz); 130.41 and 130.30 ($J_{C-F} = 8.3$ Hz); 123.69 and 123.65 ($J_{C-F} = 2.9$ Hz); 115.20 and 114.91 ($J_{C-F} = 22.3$ Hz); 114.62 and 114.34 ($J_{C-F} = 20.9$ Hz); 75.13; 47.26 and 47.24 ($J_{C-F} = 1.7$ Hz); 39.50; 21.06. **B**: 175.94; 164.33 and 161.07 ($J_{C-F} = 246.2$ Hz); 138.66 and 138.56 ($J_{C-F} = 7.4$ Hz); 130.25 and 130.14 ($J_{C-F} = 8.3$ Hz); 123.25 and 123.21 ($J_{C-F} = 2.9$ Hz); 114.85 and 114.56 ($J_{C-F} = 22.3$ Hz); 114.62 and 114.34 ($J_{C-F} = 20.9$ Hz); 74.96; 45.24 and 45.22 ($J_{C-F} = 1.7$ Hz); 37.62; 20.82. IR ($CDCl_3$): ν_{max} 1266, 1345, 1388, 1448, 1492, 1593, 1768, 2935, 2983 cm^{-1}. LRMS: *m*/*z* (%) 195 ($M^{\bullet+}$ + H, 22), 150 (52), 135 (100), 122 (17), 115 (22), 109 (17), 96 (10), 83 (3), 75 (7), 63 (5), 57 (4), 51 (7).

3-(3,4-Difluorophenyl)-5-methyltetrahydrofuran-2-one (4o). White crystals, yield 89%. Mp 29–30 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.20–6.99 m, 3H, (Ar); 4.86–4.74 m, 1H, (H5); 3.94–3.87 m, 1H, (H3); 2.57–2.46 m, 1H, (H4a); 2.42–2.32 m, 1H, (H4b); 1.47 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.21–6.99 m, 3H, (Ar); 4.70–4.57 m, 1H, (H5); 3.87 dd, 1H, $J_1 = 8.6$, $J_2 = 13.0$, (H3); 2.84–2.74 m, 1H, (H4a); 2.04–1.91 m, 1H, (H4b); 1.51 d, 3H, $J = 6.1$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.25; 133.67 and 133.61 ($J_{C-F} = 3.9$ Hz); 123.83, 123.78, 123.75 and 123.70 ($J_{C-F} = 3.4$ and 6.3 Hz); 117.66 and 117.43 ($J_{C-F} = 17.2$ Hz); 117.27 and 117.03 ($J_{C-F} = 18.0$ Hz); 74.95; 46.62; 39.36; 20.68. **B**: 175.96; 152.03, 151.87, 148.74 and 148.57 ($J_{C-F} = 248.8$ a

12.6 Hz); 151.49, 151.32, 148.19 and 148.03 (J_{C-F} = 248.5 and 12.6 Hz); 133.22 and 133.17 (J_{C-F} = 3.8 Hz); 124.22, 124.17, 124.14 and 124.09 (J_{C-F} = 3.6 and 6.4 Hz); 117.81 and 117.58 (J_{C-F} = 17.5 Hz); 116.98 and 116.74 (J_{C-F} = 18.0 Hz); 75.02; 44.43; 37.36; 20.93. IR ($CDCl_3$): ν_{max} 1289, 1345, 1388, 1433, 1522, 1611, 1770, 2935, 2983 cm^{-1}. LRMS: *m*/*z* (%) 213 ($M^{\bullet+}$ + H, 82), 195 (1), 168 (72), 153 (100), 140 (21), 133 (43), 127 (28), 114 (11), 101 (10), 81 (3), 75 (5), 63 (9), 51 (5).

3-(4-Bromophenyl)-5-methyltetrahydrofuran-2-one (4p). White crystals, yield 88%. Mp 52–53 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.86–4.73 m, 1H, (H5); 3.93–3.86 m, 1H, (H3); 2.57–2.46 m, 1H, (H4a), 2.41–2.30 m, 1H, (H4b); 1.47 d, 3H, *J* = 6.3, (–CH_3). **B**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.70–4.56 m, 1H, (H5); 3.86 dd, 1H, J_1 = 8.5, J_2 = 13.0, (H3); 2.83–2.72 m, 1H, (H4a); 2.05–1.91 m, 1H, (H4b); 1.50 d, 3H, *J* = 6.1, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.32; 135.74; 131.93; 129.26; 121.50; 75.06; 44.98; 37.65; 21.08. **B**: 176.03; 135.25; 131.80; 129.65; 121.54; 74.96; 47.12; 39.57; 20.85. IR ($CDCl_3$): ν_{max} 1266, 1344, 1388, 1456, 1491, 1770, 2935, 2982 cm^{-1}. LRMS: *m*/*z* (%) 255 ($M^{\bullet+}$, 7), 237 (1), 210 (48), 195 (10), 182 (8), 171 (3), 158 (2), 143 (1), 131 (100), 116 (66), 103 (16), 91 (20), 77 (13), 63 (10), 51 (13).

3-(3-Bromophenyl)-5-methyltetrahydrofuran-2-one (4q). Colorless oil, yield 87%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.45–7.40 m, 2H, (Ar); 7.26–7.21 m, 2H, (Ar); 4.86–4.75 m, 1H, (H5); 3.90 dd, 1H, J_1 = 7.6, J_2 = 9.2, (H3); 2.58–2.47 m, 1H, (H4a); 2.41–2.30 m, 1H, (H4b); 1.47 d, 3H, *J* = 6.3, (–CH_3). **B**: 7.45–7.40 m, 2H, (Ar); 7.26–7.21 m, 2H, (Ar); 4.69–4.56 m, 1H, (H5); 3.86 dd, 1H, J_1 = 8.5, J_2 = 12.8, (H3); 2.83–2.72 m, 1H, (H4a); 2.07–1.92 m, 1H, (H4b); 1.51 d, 3H, *J* = 6.0, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.16; 138.96; 131.01; 130.62; 130.35; 126.26; 122.81; 75.12; 45.15; 37.64; 21.06. **B**: 175.87; 138.47; 131.01; 130.62; 130.22; 126.70; 122.65; 74.99; 47.20; 39.53; 20.82. IR ($CDCl_3$): ν_{max} 1346, 1388, 1479, 1569, 1597, 1773, 2936, 2984 cm^{-1}. LRMS: *m*/*z* (%) 255 ($M^{\bullet+}$, 4), 237 (1), 223 (1), 210 (30), 195 (4), 184 (7), 169 (3), 156 (2), 131 (100), 116 (40), 103 (15), 91 (20), 77 (12), 63 (8), 51 (11).

3-(3,4-Dibromophenyl)-5-methyltetrahydrofuran-2-one (4r). White crystals, yield 83%. Mp 40–42 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.62–7.54 m, 2H, (Ar); 7.15–7.08 m, 1H, (Ar); 4.87–4.74 m, 1H, (H5); 3.91–3.84 m, 1H, (H3); 2.58–2.45 m, 1H, (H4a); 2.42–2.31 m, 1H, (H4b); 1.47 d, 3H, *J* = 6.4, (–CH_3). **B**: 7.62–7.54 m, 2H, (Ar); 7.15–7.08 m, 1H, (Ar); 4.70–4.56 m, 1H, (H5); 3.84 dd, 1H, J_1 = 8.5, J_2 = 12.9, (H3); 2.84–2.72 m, 1H, (H4a); 2.05–1.90 m, 1H, (H4b); 1.51 d, 3H, *J* = 6.1, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ **A**: 175.74; 137.55; 133.91; 132.78; 127.82; 125.20; 123.92; 75.09; 44.49; 37.34; 21.04. **B**: 175.44; 137.07; 133.79; 133.13; 128.20; 125.03; 123.92; 75.05; 46.65; 39.29; 20.78. IR ($CDCl_3$): ν_{max} 1344, 1388, 1464, 1557, 1772, 2935, 2983 cm^{-1}. LRMS: *m*/*z* (%) 334 ($M^{\bullet+}$, 4), 290 (40), 262 (7), 209 (22), 196 (23), 182 (7), 130 (100), 115 (48), 102 (27), 89 (6), 75 (11), 63 (9), 51 (11).

5-Methyl-3-(1-naphthyl)tetrahydrofuran-2-one (4s). White crystals, yield 66%. Mp 92–94 °C, lit.[31] 101–102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.92–7.78 m, 3H, (Ar); 7.60–7.34 m, 4H, (Ar); 4.85–4.71 m, 1H, (H5); 4.67–4.56 m, 1H, (H3); 2.53–2.47 m, 2H, (H4); 1.51 d, 3H, *J* = 6.3 Hz, (–CH_3); **B**: 7.92–7.78 m, 3H, (Ar); 7.60–7.34 m, 4H, (Ar); 4.85–4.71 m, 1H, (H5); 4.67–4.56 m, 1H, (H3); 1.54 d, 3H, *J* = 6.3 Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.66, 134.13, 133.37, 131.34, 129.15, 128.38, 126.56, 125.94, 125.41, 124.58, 122.98, 75.55, 43.89, 38.63, 20.91; **B**: 176.98, 134.02, 133.06, 131.03, 129.15, 128.38, 126.43, 125.79, 125.58, 124.58, 122.82, 75.21, 44.84, 39.67, 21.07. IR ($CDCl_3$): ν_{max} 2983, 2935, 1770, 1599, 1513, 1455, 1387, 1343 cm^{-1}. LRMS: 226 ($M^{\bullet+}$, 83), 198 (3), 182 (17), 167 (100), 153 (72), 139 (8), 127 (7), 115 (8), 102 (3), 89 (5), 77 (9), 63 (8), 51 (8).

5-Methyl-3-(4-bromo-1-naphthyl)tetrahydrofuran-2-one (4t). Colorless oil, yield 93%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 8.37–8.30 m, 1H, (Ar); 7.92–7.84 m, 1H, (Ar); 7.75 d, 1H, *J* = 7.7 Hz, (Ar); 7.68–7.57 m, 2H, (Ar); 7.21 d, 1H, *J* = 7.7 Hz, (Ar); 4.84–4.72 m, 1H, (H5); 4.60 dd, 1H, J_1 = 8.4 Hz, J_2 = 6.5 Hz, (H3); 2.53–2.44 m, 2H, (H4), 1.51 d, 3H, *J* = 6.3 Hz, (–CH_3); **B**: 8.37–8.30 m, 1H, (Ar); 7.93–7.86 m, 1H, (Ar); 7.79 d, 1H, *J* = 7.7 Hz, (Ar); 7.67–7.56 m, 2H, (Ar); 7.32 d, 1H, *J* = 7.7 Hz, (Ar); 4.84–4.72 m, 1H, (H5); 4.58 dd, 1H, J_1 = 12.1 Hz, J_2 = 8.8 Hz, (H3); 3.01–2.86 m, 1H, (H4a); 2.18–1.99 m, 1H, (H4b); 1.54 d, 3H, *J* = 6.3 Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.11, 133.48, 132.47, 132.29, 129.46, 128.43, 127.42, 127.39, 125.02, 123.46, 123.10, 75.52, 43.64, 38.49, 20.91; **B**: 176.45, 133.14, 132.63, 132.32, 129.70, 128.43, 127.29, 127.27, 126.10, 123.29, 123.13, 75.24, 44.66, 39.62, 21.04. IR ($CDCl_3$): ν_{max} 2982, 2935, 1767, 1595, 1508, 1384, 1345 cm^{-1}. LRMS: 304 ($M^{\bullet+}$-H, 74), 260 (13), 245 (13), 233 (20), 219 (4), 181 (100), 166 (84), 152 (55), 139 (15), 126 (10), 115 (4), 101 (4), 87 (5), 76 (6), 63 (11), 50 (7).

5-Methyl-3-[3-(*N*-methylindolyl)]tetrahydrofuran-2-one (4u). White crystals, yield 95%. Mp 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.60–7.56 m, 1H, (Ar); 7.36–7.22 m, 2H, (Ar); 7.19–7.10 m, 2H, (Ar); 4.86–4.73 m, 1H, (H5); 4.17 dd, 1H, J_1 = 12.4 Hz, J_2 = 8.6 Hz, (H3); 3.75 s, 3H, (N–CH_3); 2.65–2.53 m, 1H, (H4a); 2.45–2.32 m, 1H, (H4b); 1.49 d, 3H, *J* = 6.3 Hz, (–CH_3); **B**: 7.55–7.51 m, 1H, (Ar); 7.36–7.22 m, 2H, (Ar); 7.19–7.10 m, 2H, (Ar); 4.73–4.62 m, 1H, (H5); 4.17 dd, 1H, J_1 = 12.4 Hz, J_2 = 8.6 Hz, (H3), 3.76 s, 3H, (N–CH_3); 2.94–2.81 m, 1H, (H4a); 2.13–1.98 m, 1H, (H4b); 1.51 d, 3H, *J* = 6.0 Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.65, 137.25, 126.63, 126.52, 122.04, 119.31, 118.79, 109.54, 75.46, 39.24, 37.49, 32.70, 20.93; **B**: 177.36, 137.12, 126.94, 126.44, 121.89, 119.23, 118.75,

109.54, 75.18, 39.47, 37.74, 32.70, 20.93. IR ($CDCl_3$): ν_{max} 2982, 2936, 1766, 1476, 1388, 1342, 1255 cm^{-1}. LRMS: 229 ($M^{\bullet+}$, 6), 185 (10), 170 (26), 157 (6), 144 (7), 130 (3), 115 (3), 102 (2), 89 (2), 77 (1), 63 (2), 51 (1).

5-Methyl-3-(1-adamantyl)tetrahydrofuran-2-one (4w). White crystals, yield 68%. Mp 66–68 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 4.60–4.48 m, 1H, (H5); 2.40–2.28 m, 2H, (H3 + H4a); 2.28–2.14 m, 1H, (H4b); 2.05–1.95 m, 3H, (CH); 1.95–1.45 m, 12H, (CH_2); 1.34 d, 3H, $J = 6.2$ Hz, (–CH_3); **B**: 4.44–4.30 m, 1H, (H5); 2.40–2.28 m, 2H, (H3 + H4a); 2.28–2.14 m, 1H, (H4b); 2.05–1.95 m, 3H, (CH); 1.95–1.45 m, 12H, (CH_2); 1.39 d, 3H, $J = 6.2$ Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.18, 74.69, 51.54, 39.54, 36.84, 34.66, 31.83, 28.31, 21.72; **B**: 176.62, 73.83, 49.90, 39.24, 36.71, 33.58, 30.46, 28.31, 20.88. IR ($CDCl_3$): ν_{max} 2908, 2852, 1759, 1528, 1453, 1344, 1284 cm^{-1}. LRMS: 235 ($M^{\bullet+}$ + H, 52), 189 (4), 161 (4), 136 (10), 135 (100), 107 (5), 105 (6), 93 (5), 91 (8), 79 (5), 67 (3), 55 (5), 53 (3).

Preparation of tetrahydrofuranes 4c, 4d and 4v. A solution of HBr in AcOH (30 wt%, 10 mL) was slowly added to 2-substituted pent-4-enoic acid (**3c**, **3d**, **3v**) (8.0 mmol) placed under Ar. The reaction mixture was stirred for 6 h, and the solvent was then removed. The residue was redissolved in methanol (15 mL), and Na_2CO_3 (16 mmol) was added to the solution. After stirring for 45 min at ambient temperature, the solution was diluted with brine, and the resultant mixture extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, and the solvent evaporated. Purification by column chromatography (petroleum ether–ether 85:15) afforded lactones **4c**, **4d** and **4u** in 71–86% yields.

3-(4-Methoxyphenyl)-5-methyltetrahydrofuran-2-one (4c). White crystals, yield 71%. Mp 68–70 °C. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.23–7.17 m, 2H, (AA′BB′); 6.93–6.86 m, 2H, (AA′BB′); 4.85–4.73 m, 1H, (H5); 3.88 dd, 1H, $J_1 = 7.4$, $J_2 = 9.2$, (H3); 3.80 s, 3H, (–OCH_3); 2.56–2.46 m, 1H, (H4a); 2.38–2.27 m, 1H, (H4b); 1.46 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.23–7.17 m, 2H, (AA′BB′); 6.93–6.86 m, 2H, (AA′BB′); 4.67–4.54 m, 1H, (H5); 3.84 dd, 1H, $J_1 = 8.6$, $J_2 = 12.8$, (H3); 3.80 s, 3H, (–OCH_3); 2.81–2.70 m, 1H, (H4a); 2.06–1.91 m, 1H, (H4b); 1.50 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.23; 158.77; 128.82; 128.38; 114.26; 75.03; 55.32; 44.85; 38.03; 21.11. **B**: 176.97; 158.80; 128.99; 128.56; 114.15; 74.82; 55.32; 46.99; 39.89; 20.91. IR ($CDCl_3$): ν_{max} 1515, 1585, 1614, 1770, 2839, 2936, 2982 cm^{-1}. LRMS: *m/z* (%) 206 ($M^{\bullet+}$, 27), 162 (29), 148 (28), 147 (100), 134 (11), 119 (14), 103 (8), 90 (13), 91 (50), 77 (17), 65 (15), 51 (18).

3-(3-Methoxyphenyl)-5-methyltetrahydrofuran-2-one (4d). Colorless oil, yield 81%. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.31–7.24 m, 1H, (Ar); 6.89–6.80 m, 3H, (Ar); 4.86–4.74 m, 1H, (H5); 3.90 dd, 1H, $J_1 = 7.1$, (H3); 3.80 s, 3H, (Ar–OCH_3); 2.59–2.48 m, 1H, (H4a); 2.39–2.28 m, 1H, (H4b); 1.46 d, 3H, $J = 6.3$, (–CH_3). **B**: 7.31–7.24 m, 1H, (Ar); 6.89–6.80 m, 3H, (Ar); 4.68–4.55 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.7$, $J_2 = 12.7$, (H3); 3.80 s, 3H, (Ar–OCH_3); 2.82–2.71 m, 1H, (H4a); 2.09–1.95 m, 1H, (H4b); 1.50 d, 3H, $J = 6.3$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.99; 159.90; 138.44; 129.93; 119.78; 113.53; 112.81; 75.18; 55.19; 45.64; 37.85; 20.96. **B**: 176.68; 159.79; 137.95; 129.79; 120.28; 113.97; 112.83; 74.89; 55.19; 47.60; 39.65; 20.76. IR ($CDCl_3$): ν_{max} 1156, 1246, 1299, 1468, 1603, 1764, 2838, 2981, 2999 cm^{-1}. LRMS: *m/z* (%) 206 ($M^{\bullet+}$, 72), 205 (2), 191 (1), 178 (12), 162 (32), 147 (100), 131 (29), 121 (17), 115 (17), 103 (12), 91 (63), 77 (17), 65 (19), 55 (4), 51 (13).

5-Methyl-3-(3-benzo[b]thienyl)tetrahydrofuran-2-one (4v). Colorless oil, yield 86%. ^1H NMR (300 MHz, $CDCl_3$): δ **A**: 7.77–7.67 (2H, m, Ar5,7), 7.45–7.34 m, 3H, (Ar2,4,6); 4.88–4.66 m, 1H, (H5); 4.27 dd, 1H, $J_1 = 12.4$ Hz, $J_2 = 8.8$ Hz, (H3); 2.63–2.52 m, 1H, (H4a); 2.47–2.35 m, 1H, (H4b); 1.50 d, 3H, $J = 6.3$ Hz, (–CH_3); **B**: 7.90–7.85 m, 2H, (Ar5,7); 7.45–7.34 m, 3H, (Ar2,4,6); 4.88–4.66 m, 1H, (H5); 4.27 dd, 1H, $J_1 = 12.4$ Hz, $J_2 = 8.8$ Hz, (H3); 2.95–2.83 m, 1H, (H4a); 2.16–2.00 m, 1H, (H4b); 1.53 d, 3H, $J = 6.3$ Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.32, 140.56, 137.55, 130.98, 124.70, 124.31, 123.89, 123.06, 121.58, 75.57, 40.55, 36.82, 20.92; **B**: 175.89, 140.55, 137.67, 130.74, 124.55, 124.21, 123.89, 123.05, 121.52, 75.25, 41.90, 38.27, 20.88. IR ($CDCl_3$): ν_{max} 2984, 2935, 1771, 1430, 1388, 1343 cm^{-1}. LRMS: 232 ($M^{\bullet+}$, 6), 188 (26), 173 (78), 160 (7), 147 (14), 129 (10), 115 (22), 102 (4), 89 (5), 77 (3), 63 (5), 50 (4).

Preparation of furanones 5a–u and 5w. Butyllithium (5.5 mmol) was added to a solution of diisopropylamine (5.3 mmol) in dry THF (15 mL) at 0 °C under argon. After 10 min at 0 °C, the LDA solution was cooled to −60 °C, and a solution of a saturated lactone (**4a–u**, **4w**) (5.0 mmol) in THF (2 mL) was added. The reaction temperature was maintained at −60 °C for 30 min, and a solution of phenylselenenyl chloride (7.5 mmol) in THF (5 mL) was added. The resultant mixture was slowly allowed to warm to room temperature (over 2 h), diluted with ethyl acetate (50 mL), washed with saturated aqueous NH_4Cl, dried over Na_2SO_4, and concentrated. The crude phenylselanyl derivative was rapidly purified by column chromatography (petroleum ether–ether 98:2), dissolved in $CHCl_3$ (10 mL), and MCPBA (7.5 mmol) or H_2O_2 (30%, 2–6 mL) were added to the solution in several portions at 0 °C. The reaction mixture was then stirred for 2 h at ambient temperature or until TLC indicated the reaction was complete. A further portion of $CHCl_3$ (10 mL) was added along with 5% aqueous Na_2CO_3 (20 mL). The layers were separated, the organic phase was washed with 5% aqueous Na_2CO_3 (20 mL), dried over Na_2SO_4, and the solvent evaporated. Products **5a–w** were purified by column chromatography (petroleum ether–ether 9:1), and were obtained with overall yields in the range 13–65% over two steps.

3-Phenyl-5-methyl-2,5-dihydrofuran-2-one (5a). White crystals, yield 62%. Mp 45–46 °C, lit.[8] 47–48 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88–7.83 m, 2H, (Ar); 7.55 d, 1H, $J = 1.9$, (H4); 7.46–7.38 m, 3H, (Ar); 5.16 qd, H, $J_1 = 1.9$, $J_2 = 6.9$, (H5); 1.52 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.66; 148.92; 131.39; 129.48; 129.31; 128.64; 127.03; 76.71; 19.15. IR ($CDCl_3$): ν_{max} 1322, 1375, 1450, 1493, 1758, 2986 cm^{-1}. LRMS: *m*/*z* (%) 174 ($M^{\bullet+}$, 65), 131 (25), 128 (6), 115 (5), 104 (25), 103 (100), 102 (12), 89 (3), 77 (14), 63 (8), 51 (15). calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79; found: C, 75.60; H, 5.75.

3-(4-Methylphenyl)-5-methyl-2,5-dihydrofuran-2-one (5b). White crystals, yield 51%. Mp 55–57 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78–7.72 m, 2H, (AA′BB′); 7.49 d, 1H, $J = 1.9$, (H4); 7.25–7.19 m, 2H, (AA′BB′), 5.14 qd, 1H, $J_1 = 6.9$, $J_2 = 1.9$, (H5); 2.38 s, 3H, (CH_3–Ar); 1.51 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.83; 147.95; 139.39; 131.20; 129.32; 126.89; 126.64; 76.65; 21.35; 19.19. IR ($CDCl_3$): ν_{max} 1322, 1513, 1753, 2933, 3032 cm^{-1}. LRMS: *m*/*z* (%) 188 ($M^{\bullet+}$, 73), 145 (20), 128 (8), 118 (33), 117 (100), 115 (44), 102 (3), 91 (12), 77 (5), 63 (10), 51 (11). calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43; found: C, 76.52; H, 6.42.

3-(4-Methoxyphenyl)-5-methyl-2,5-dihydrofuran-2-one (5c). White crystals, yield 45%. Mp 63–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83–7.77 m, 2H, (AA′BB′); 7.43 d, 1H, $J = 1.9$, (H4); 6.95–6.89 m, 2H, (AA′BB′); 5.13 qd, 1H, $J_1 = 1.9$, $J_2 = 6.9$, (H5); 3.82 s, 3H, (–OCH_3); 1.49 d, 3H, $J = 6.9$ Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 172.25; 160.32; 146.97; 130.60; 128.36; 121.96; 113.97; 76.80; 55.27; 19.14. IR ($CDCl_3$): ν_{max} 1257, 1306, 1442, 1512, 1608, 1751, 2840, 2935, 2986 cm^{-1}. LRMS: *m*/*z* (%) 204 ($M^{\bullet+}$, 67), 176 (6), 161 (12), 145 (6), 134 (37), 133 (100), 115 (9), 102 (9), 89 (13), 77 (10), 63 (12), 51 (10). calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92; found: C, 70.45; H, 5.96.

3-(3-Methoxyphenyl)-5-methyl-2,5-dihydrofuran-2-one (5d). Colorless oil, yield 50%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 d, 1H, $J = 1.8$, (H4); 7.46–7.25 m, 3H, (Ar); 6.95–6.90 m, 1H, (Ar); 5.14 qd, 1H, $J_1 = 1.8$, $J_2 = 6.8$, (H5); 3.83 s, 3H, (Ar–OCH_3); 1.50 d, 3H, $J = 6.8$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.53; 159.63; 149.30; 131.07; 130.70; 129.61; 119.36; 115.08; 112.30; 76.64; 55.27; 19.06. IR ($CHCl_3$): ν_{max} 1318, 1432, 1466, 1489, 1580, 1601, 1755, 2838, 2936, 3012, 3027 cm^{-1}. LRMS: *m*/*z* (%) 205 ($M^{\bullet+}$ + H, 100), 187 (2), 175 (1), 161 (12), 145 (2), 133 (28), 118 (10), 102 (7), 89 (8), 77 (1), 63 (5), 51 (2). calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92; found: C, 70.79; H, 6.16.

3-(4-Nitrophenyl)-5-methyl-2,5-dihydrofuran-2-one (5e). Yellow crystals, yield 56%. Mp 133–135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.29–8.22 m, 2H, (AA′BB′); 8.09–8.03 m, 2H, (AA′BB′); 7.78 d, 1H, $J = 1.7$, (H4); 5.23 qd, 1H, $J_1 = 1.7$, $J_2 = 6.9$, (H5); 1.56 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.51; 152.14; 147.86; 135.43; 129.53; 127.82; 123.73; 77.08; 18.99. IR (KBr pellet): ν_{max} 856, 976, 1136, 1345, 1511, 1600, 1743, 2983, 3074 cm^{-1}. LRMS: *m*/*z* (%) 219 ($M^{\bullet+}$, 100), 203 (14), 189 (7), 160 (9), 148 (79), 132 (13), 118 (20), 102 (28), 90 (19), 75 (18), 63 (13), 51 (18). calcd for $C_{11}H_9NO_4$: C, 60.28; H, 4.14; N 6.39; found: C, 60.28; H, 4.08; N 6.39.

3-(4-Trifluoromethylphenyl)-5-methyl-2,5-dihydrofuran-2-one (5f). White crystals, yield 48%. Mp 91–93 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00–7.95 m, 2H, (AA′BB′); 8.69–7.64 m, 2H, (AA′BB′); 7.67 d, 1H, $J = 1.8$, (H4); 5.20 qd, 1H, $J_1 = 1.8$, $J_2 = 6.9$, (H5); 1.54 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.09; 151.22; 132.89, 132.87, 132.85 and 132.83 ($J_{C-F} = 1.3$ Hz); 131.42, 130.99, 130.56 and 130.13 ($J_{C-F} = 32.6$ Hz); 129.93; 129.20, 125.59, 121.98 and 118.38 ($J_{C-F} = 272.2$ Hz); 127.25; 125.43, 125.38, 125.33 and 125.28 ($J_{C-F} = 3.8$ Hz); 76.94; 18.73. IR (KBr pellet): ν_{max} 848, 979, 1072, 1116, 1328, 1416, 1617, 1750 cm^{-1}. LRMS: *m*/*z* (%) 242 ($M^{\bullet+}$, 80), 223 (11), 213 (2), 199 (30), 171 (100), 151 (33), 145 (5), 120 (6), 102 (7), 87 (3), 75 (8), 63 (5), 50 (7). calcd for $C_{12}H_9F_3O_2$: C, 59.51; H, 3.75; found: C, 59.76; H, 3.85.

3-(3-Trifluoromethylphenyl)-5-methyl-2,5-dihydrofuran-2-one (5g). White crystals, yield 55%. Mp 39–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13–8.06 m, 2H, (Ar); 7.66 d, 1H, $J = 1.9$, (H4); 7.64–7.50 m, 2H, (Ar); 5.19 qd, 1H, $J_1 = 1.9$, $J_2 = 6.9$, (H5); 1.54 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.90; 150.18; 131.64, 131.20, 130.78 and 130.34 ($J_{C-F} = 32.6$ Hz); 130.21, 130.19, 130.17 and 130.15 ($J_{C-F} = 1.3$ Hz); 130.14; 130.11; 129.14, 125.54, 121.94 and 118.34 ($J_{C-F} = 271.8$ Hz); 129.11; 125.87, 125.82, 125.77 and 125.73 ($J_{C-F} = 3.7$ Hz); 123.84, 123.79, 123.74 and 123.68 ($J_{C-F} = 3.9$ Hz); 76.89; 19.12. IR ($CDCl_3$): ν_{max} 1268, 1336, 1346, 1451, 1488, 1758, 2935, 2987 cm^{-1}. LRMS: *m*/*z* (%) 243 ($M^{\bullet+}$ + H, 100), 223 (4), 199 (5), 171 (8), 151 (10), 128 (2), 102 (3), 75 (2), 63 (2), 51 (2). calcd for $C_{12}H_9F_3O_2$: C, 59.51; H, 3.75; found: C, 59.48; H, 3.91.

3-(4-Chlorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5h). White crystals, yield 56%. Mp 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.78 m, 2H, (AA′BB′); 7.55 d, 1H, $J = 1.9$, (H4); 7.41–7.36 m, 2H, (AA′BB′); 5.15 qd, 1H, $J_1 = 6.9$, $J_2 = 1.9$, (H5); 1.52 d, 3H, $J = 6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.18; 148.99; 135.22; 130.19; 128.76; 128.22; 127.79; 76.77; 19.17. IR (KBr pellet): ν_{max} 834, 977, 1093, 1144, 1322, 1492, 1745, 2993 cm^{-1}. LRMS: *m*/*z* (%) 208 ($M^{\bullet+}$ − H, 52), 165 (23), 139 (38), 137 (100), 127 (5), 115 (11), 101 (22), 87 (4), 75 (18), 63 (11), 51 (18). calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35; found: C, 63.14; H, 4.50.

3-(3-Chlorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5i). White crystals, yield 62%. Mp 50–51°. ^{1}H NMR

(300 MHz, $CDCl_3$): δ 7.86–7.83 m, 1H, (Ar); 7.79–7.72 m, 1H, (Ar); 7.59 d, 1H, $J=1.9$, (H4); 7.36–7.33 m, 2H, m, (Ar); 5.16 qd, 1H, $J_1=1.9$, $J_2=6.9$, (H5); 1.52 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.15; 150.06; 134.71; 131.23; 130.32; 130.01; 129.46; 127.19; 125.26; 77.21; 19.34. IR ($CDCl_3$): ν_{max} 1321, 1476, 1568, 1595, 1755, 2935, 2987, 3075 cm^{-1}. LRMS: *m*/*z* (%) 209 ($M^{\bullet+}$, 100), 191 (3), 165 (13), 137 (36), 115 (7), 102 (18), 87 (2), 75 (8), 63 (6), 51 (8). calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35; found: C, 63.47; H, 4.62.

3-(2-Chlorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5j). White crystals, yield 59%. Mp 59–60 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 d, 1H, $J=1.7$, (H4); 7.68–7.64 m, 1H, (Ar); 7.47–7.43 m, 1H, (Ar); 7.34–7.29 m, 2H, (Ar); 5.22 qd, 1H, $J_1=1.7$, $J_2=6.9$, (H5); 1.55 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.43; 154.33; 132.97; 130.65; 129.99; 129.88; 129.83; 129.14; 126.70; 77.22; 19.09. IR ($CDCl_3$): ν_{max} 1320, 1376, 1438, 1451, 1477, 1760, 2935, 2986 cm^{-1}. LRMS: *m*/*z* (%) 208 ($M^{\bullet+}-H$, 53), 191 (2), 173 (7), 165 (46), 145 (7), 137 (100), 128 (9), 115 (11), 101 (25), 87 (3), 75 (18), 63 (8), 51 (14). calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35; found: C, 63.18; H, 4.54.

3-(3,4-Dichlorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5k). White crystals, yield 60%. Mp 110–111 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 d, 1H, $J=1.9$, (Ar); 7.73 dd, 1H, $J_1=8.4$, $J_2=1.9$, (Ar); 7.60 d, 1H, $J=1.9$, (H4); 7.48 d, 1H, $J=8.4$, (Ar); 5.17 qd, 1H, $J_1=6.9$, $J_2=1.9$, (H5); 1.53 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.71; 150.15; 133.18; 132.65; 130.39; 129.17; 128.95; 128.61; 126.05; 76.87; 18.98. IR ($CHCl_3$): ν_{max} 1323, 1383, 1472, 1552, 1758, 2935, 2988, 3026 cm^{-1}. LRMS: *m*/*z* (%) 242 ($M^{\bullet+}-H$, 100), 225 (4), 214 (3), 199 (33), 171 (94), 150 (7), 136 (31), 126 (7), 115 (9), 99 (13), 86 (6), 74 (13), 63 (9), 50 (14). calcd for $C_{11}H_8Cl_2O_2$: C, 54.35; H, 3.32; found: C, 54.56; H, 3.25.

3-(2,4-Dichlorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5l). White crystals, yield 36%. Mp 47–49 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 d, 1H, $J=1.7$, (H4); 7.65 d, 1H, $J=8.5$, (Ar); 7.47 d, 1H, $J=2.2$, (Ar); 7.31 dd, 1H, $J_1=2.2$, $J_2=8.5$, (Ar); 5.21 qd, 1H, $J_1=1.7$, $J_2=6.9$, (H5); 1.54 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.17; 154.61; 135.14; 133.71; 131.41; 129.85; 128.05; 127.10; 126.68; 77.30; 19.02. IR (KBr pellet): ν_{max} 1063, 1116, 1136, 1319, 1476, 1586, 1755, 2933, 2982 cm^{-1}. LRMS: *m*/*z* (%) 242 ($M^{\bullet+}-H$, 49), 199 (29), 174 (72), 171 (100), 149 (5), 136 (21), 127 (8), 115 (7), 98 (17), 86 (7), 74 (18), 62 (11), 50 (17). calcd for $C_{11}H_8Cl_2O_2$: C, 54.35; H, 3.32; found: C, 54.16; H, 3.43.

3-(4-Fluorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5m). White crystals, yield 56%. Mp 81–83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90–7.80 m, 2H, (AA′BB′); 7.51 d, 1H, $J=1.9$, (H4); 7.15–7.00 m, 2H, (AA′BB′), 5.13 qd, 1H, $J_1=6.9$, $J_2=1.9$, (H5); 1.48 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.37; 164.60 and 161.30 ($J_{C-F}=249.1$ Hz); 148.54 and 148.52 ($J_{C-F}=1.7$ Hz); 130.00; 128.85 and 128.74 ($J_{C-F}=8.3$ Hz); 125.52 and 125.47 ($J_{C-F}=3.4$ Hz); 115.62 and 115.33 ($J_{C-F}=21.5$ Hz); 76.70; 19.08. IR (KBr pellet): ν_{max} 834, 974, 1117, 1224, 1300, 1323, 1457, 1508, 1602, 1746, 2879, 2988 cm^{-1}. LRMS: *m*/*z* (%) 192 ($M^{\bullet+}$, 55), 175 (2), 164 (4), 149 (28), 133 (9), 127 (3), 121 (100), 115 (4), 107 (3), 101 (21), 87 (3), 81 (3), 75 (10), 62 (5), 57 (5), 50 (8). calcd for $C_{11}H_9FO_2$: C, 68.75; H, 4.72; found: C, 68.49; H, 4.78.

3-(3-Fluorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5n). White crystals, yield 65%. Mp 43–45 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70–7.55 m, 2H, (Ar); 7.59 d, 1H, $J=1.9$, (H4); 7.45–7.30 m, 1H, (Ar); 7.07 tdd, 1H, $J_1=8.3$, $J_2=2.6$, $J_3=1.0$, (Ar); 5.16 qd, 1H, $J_1=6.9$, $J_2=1.9$, (H5); 1.51 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.99; 164.21 and 160.96 ($J_{C-F}=245.6$ Hz); 149.81; 131.38 and 131.26 ($J_{C-F}=8.3$ Hz); 130.12 and 130.01 ($J_{C-F}=8.0$ Hz); 122.61 and 122.57 ($J_{C-F}=3.2$ Hz); 116.26 and 115.98 ($J_{C-F}=21.2$ Hz); 114.12 and 113.81 ($J_{C-F}=23.2$ Hz); 76.75; 19.10. IR ($CDCl_3$): ν_{max} 1273, 1317, 1450, 1488, 1585, 1758, 2935, 2986 cm^{-1}. LRMS: *m*/*z* (%) 192 ($M^{\bullet+}$, 71), 163 (3), 149 (31), 133 (9), 121 (100), 115 (5), 101 (20), 81 (3), 75 (9), 62 (5), 50 (7). calcd for $C_{11}H_9FO_2$: C, 68.75; H, 4.72; found: C, 68.96; H, 4.89.

3-(3,4-Difluorophenyl)-5-methyl-2,5-dihydrofuran-2-one (5o). White crystals, yield 60%. Mp 107–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81–7.72 m, 1H, (Ar); 7.65–7.58 m, 1H, (Ar); 7.55 d, 1H, $J=1.7$, (H4); 7.25–7.15 m, 1H, (Ar); 5.16 qd, 1H, $J_1=1.7$, $J_2=6.9$, (H5); 1.52 d, 3H, $J=6.9$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.12; 152.64, 152.48, 149.31 and 149.15 ($J_{C-F}=251.4$ and 12.0 Hz); 152.02, 151.85, 148.73 and 148.56 ($J_{C-F}=248.1$ and 12.5 Hz); 149.44 and 149.41 ($J_{C-F}=1.7$ Hz); 129.44; 126.46, 126.40, 126.37 and 126.32 ($J_{C-F}=4.1$ and 6.6 Hz); 123.53, 123.48, 123.44 and 123.39 ($J_{C-F}=3.7$ and 6.3 Hz); 117.69 and 117.46 ($J_{C-F}=17.5$ Hz); 116.41 and 116.16 ($J_{C-F}=18.9$ Hz); 76.77; 19.01. IR ($CDCl_3$): ν_{max} 1275, 1319, 1376, 1436, 1518, 1604, 1754, 2935, 2986 cm^{-1}. LRMS: *m*/*z* (%) 210 ($M^{\bullet+}$, 65), 193 (2), 182 (4), 167 (30), 151 (7), 139 (100), 119 (21), 99 (8), 87 (6), 74 (5), 63 (8), 50 (5). calcd for $C_{11}H_8F_2O_2$: C, 62.86; H, 3.84; found: C, 62.75; H, 4.00.

3-(4-Bromophenyl)-5-methyl-2,5-dihydrofuran-2-one (5p). White crystals, yield 58%. Mp 105–106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78–7.71 m, 2H, (AA′BB′); 7.56 d, 1H, $J=1.9$, (H4); 7.56–7.52 m, 2H, (AA′BB′); 5.15 qd, 1H, $J_1=1.9$, $J_2=6.8$ Hz, (H5); 1.52 d, 3H, $J=6.8$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.10; 149.05; 131.73; 130.29; 128.47; 128.23; 123.57; 76.79; 19.16. IR ($CDCl_3$): ν_{max} 1296, 1323, 1403, 1488, 1590, 1757, 2987 cm^{-1}. LRMS: *m*/*z* (%) 254 ($M^{\bullet+}+H$, 69), 223 (4), 209 (30), 195 (9), 181 (100), 144 (4), 128 (12), 115 (18), 102 (55), 91 (7), 75 (38), 63 (17), 51 (39). calcd for $C_{11}H_9BrO_2$: C, 52.20; H, 3.58; found: C, 52.39; H, 3.52.

3-(3-Bromophenyl)-5-methyl-2,5-dihydrofuran-2-one (5q). White crystals, yield 61%. Mp 58–59 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 bs, 1H, (Ar); 7.81 bd, 1H, J = 7.8, (Ar); 7.58 d, 1H, J = 1.7, (H4); 7.51 bd, 1H, J = 7.8, (Ar); 7.28 bt, 1H, J = 7.8, (Ar); 5.16 qd, 1H, J_1 = 1.7, J_2 = 6.9, (H5); 1.52 d, 3H, J = 6.9, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.91; 149.85; 132.17; 131.29; 130.07; 130.03; 129.84; 125.52; 122.63; 76.79; 19.15. IR ($CDCl_3$): ν_{max} 1321, 1474, 1561, 1592, 1754, 2935, 2988 cm^{-1}. LRMS: *m*/*z* (%) 253 ($M^{\bullet+}$, 100), 237 (5), 223 (3), 209 (60), 195 (5), 181 (95), 156 (3), 145 (9), 128 (13), 115 (17), 102 (100), 87 (6), 75 (32), 63 (20), 50 (30). calcd for $C_{11}H_9BrO_2$: C, 52.20; H, 3.58; found: C, 52.32; H, 3.71.

3-(3,4-Dibromophenyl)-5-methyl-2,5-dihydrofuran-2-one (5r). White crystals, yield 47%. Mp 103–104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 d, 1H, J = 2.0, (Ar); 7.70 dd, 1H, J_1 = 2.0, J_2 = 8.5, (Ar); 7.65 d, 1H, J = 8.5, (Ar); 7.61 d, 1H, J = 1.7, (H4); 5.16 qd, 1H, J_1 = 1.7, J_2 = 6.9, (H5); 1.52 d, 3H, J = 6.9, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.85; 150.15; 133.82; 131.94; 130.02; 129.31; 126.94; 125.89; 125.20; 76.88; 18.98. IR ($CDCl_3$): ν_{max} 1321, 1377, 1463, 1546, 1755, 2854, 2932, 2987 cm^{-1}. LRMS: *m*/*z* (%) 332 ($M^{\bullet+}$, 89), 304 (5), 289 (55), 261 (100), 223 (5), 207 (3), 193 (4), 180 (29), 128 (11), 115 (28), 101 (27), 87 (7), 74 (29), 63 (14), 50 (28). calcd for $C_{11}H_8Br_2O_2$: C, 39.80; H, 2.43; found: C, 39.99; H, 2.58.

5-Methyl-3-(1-naphthyl)-2,5-dihydrofuran-2-one (5s). White crystals, yield 39%. Mp 69–71 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94–7.85 (3H, m, Ar), 7.60–7.47 (4H, m, Ar), 7.53 (1H, d, J = 1.7 Hz, H4), 5.28 (1H, qd, J_1 = 6.9 Hz, J_2 = 1.7 Hz, H5), 1.59 (3H, d, J = 6.9 Hz, –CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.33, 153.70, 131.76, 131.03, 129.42, 128.58, 127.45, 127.27, 126.53, 125.99, 125.07, 124.40, 77.49, 19.18. IR ($CDCl_3$): ν_{max} 3063, 2985, 1754, 1591, 1509, 1319 cm^{-1}. LRMS: 224 ($M^{\bullet+}$, 100), 207 (7), 181 (14), 165 (5), 153 (16), 152 (16), 126 (3), 102 (2), 76 (3), 63 (4), 50 (3). calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39; found: C, 80.36; H, 5.26.

5-Methyl-3-(4-bromo-1-naphthyl)-2,5-dihydrofuran-2-one (5t). White crystals, yield 19%. Mp 59–61 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35–8.30 (1H, m, Ar), 7.91–7.86 (1H, m, Ar), 7.83 (1H, m, J = 7.8 Hz, Ar), 7.68–7.54 (2H, m, Ar), 7.58 (1H, d, J = 1.7 Hz, H4), 7.42 (1H, d, J = 7.8 Hz, Ar), 5.33 (1H, qd, J_1 = 6.9 Hz, J_2 = 1.7 Hz, H5), 1.63 (3H, d, J = 6.9 Hz, –CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.21, 154.18, 132.25, 132.12, 131.52, 129.36, 127.93, 127.72, 127.55, 127.43, 127.34, 124.99, 124.57, 77.79, 19.23. IR ($CDCl_3$): ν_{max} 2987, 2934, 1756, 1567, 1507, 1380, 1320 cm^{-1}. LRMS: 302 ($M^{\bullet+}$ −H, 100), 260 (43), 231 (43), 195 (3), 181 (17), 165 (13),152 (82), 126 (6), 100 (5), 87 (5), 75 (10), 63 (10), 50 (9). calcd for $C_{15}H_{11}BrO_2$: C, 59.43; H, 3.66; found: C, 59.21; H, 3.77.

5-Methyl-3-[3-(*N*-methylindolyl)]-2,5-dihydrofuran-2-one (5u). Colorless crystals, yield 25%. Mp 89–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 s, 1H, (Ar2); 7.84–7.76 m, 1H, (Ar7); 7.47 d, 1H, J = 1.9 Hz, (H4); 7.41–7.21 m, 3H, (Ar4,5,6); 5.23 qd, 1H, J_1 = 6.6 Hz, J_2 = 1.9 Hz, (H5); 3.82 s, 3H, (–NCH_3); 1.54 d, 3H, J = 6.6 Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.19, 141.08, 137.06, 130.62, 126.12, 125.70, 122.34, 120.54, 119.53, 109.90, 104.46, 77.84, 33.03, 19.60. IR ($CDCl_3$): ν_{max} 3127, 2984, 2934, 1747, 1643, 1524, 1474, 1376, 1319 cm^{-1}. LRMS: 227 ($M^{\bullet+}$, 100), 198 (2), 184 (3), 156 (46), 127 (1), 115 (5), 89 (1), 63 (1). calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16; found: C, 73.73; H, 6.06; N, 5.93.

5-Methyl-3-(1-adamantyl)-2,5-dihydrofuran-2-one (5w). White crystals, yield 13%. Mp 76–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.87 d, 1H, J = 1.7 Hz, (H4); 4.92 qd, 1H, J_1 = 6.9 Hz, J_2 = 1.7 Hz, (H5); 2.07–1.98 m, 3H, (CH); 1.88 d, 6H, J = 3.0 Hz, (CH_2), 1.76–1.71 m, 6H, (CH_2); 1.38 d, 3H, J = 6.9 Hz, (CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.90, 147.39, 142.12, 76.47, 39.76, 36.57, 33.47, 28.05, 19.32. IR ($CDCl_3$): ν_{max} 2982, 2908, 2852, 1748, 1453, 1320 cm^{-1}. LRMS: 233 ($M^{\bullet+}$ + H, 100), 217 (5), 199 (2), 189 (20), 191 (15), 175 (3), 161 (7), 145 (5), 135 (17), 117 (5), 105 (8), 91 (10), 79 (6), 65 (4), 53 (5). calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68; found: C, 77.17; H, 8.86.

5-Methyl-3-(3-benzo[b]thienyl)-2,5-dihydrofuran-2-one (5v). The introduction of the phenylselanyl moiety was identical to the above procedure for compounds **5a–u**, and **5w**. 5-Methyl-3-(3-benzo[b]thienyl)-3-phenylselanyltetrahydrofuran-2-one (1.162 g, 3 mmol) was dissolved in a mixture of MeOH–THF–H_2O 5:5:1 (50 mL), and $NaHCO_3$ (0.630 g, 7.5 mmol) and $NaIO_4$ (3.208 g, 15 mmol) were added to the solution. After stirring for 2.5 h at ambient temperature, the mixture was diluted with H_2O (50 mL), and extracted with ethyl acetate (3×). The combined extracts were dried over Na_2SO_4, and the solvent evaporated. The product was purified by column chromatography (petroleum ether–ethyl acetate 9:1), and was obtained as colourless crystals in 18% yield.

Mp 92–94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 s, 1H, (Ar2); 7.97–7.90 m, 2H, (Ar5,7); 7.70 d, 1H, J = 1.7 Hz, (H4); 7.49–7.37 m, 2H, (Ar4,6); 5.26 qd, 1H, J_1 = 6.9 Hz, J_2 = 1.7 Hz, (H5); 1.57 d, 3H, J = 6.9 Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.21, 147.06, 140.07, 137.00, 129.11, 126.04, 124.77, 124.66, 124.61, 123.16, 121.99, 77.35, 19.25. IR ($CDCl_3$) ν_{max}: 3116, 2986, 1758, 1636, 1425, 1319 cm^{-1}. LRMS: 230 ($M^{\bullet+}$, 92), 202 (9), 187 (23), 171 (6), 159 (100), 139 (3), 127 (4), 115 (54), 89 (5), 63 (8), 50 (6). calcd for $C_{13}H_{10}O_2S$: C, 67.80; H, 4.38; S, 13.92; found: C, 67.72; H, 4.48; S, 13.69.

Preparation of 3-(substituted phenyl)-5-ethyltetrahydrofuran-2-ones (6b, h, i, k, p) and 3-(substituted phenyl)-5-butyltetrahydrofuran-2-ones (8h, i, k, p). Butyllithium (11.0 mmol) was added to a solution of diisopropylamine (10.5 mmol) in dry THF (50 mL) at 0 °C under Ar.

After 10 min at 0 °C, the LDA solution was cooled to −60 °C, and a solution of a methyl (substituted phenyl)-acetate (10 mmol) in THF (5 mL) was added. The reaction temperature was maintained at −60 °C for 30 min, and epoxybutane or epoxyhexane (15.0 mmol) and boron trifluoride etherate (15.0 mmol) were subsequently added dropwise. The reaction mixture was slowly allowed to warm to room temperature (over 2.5 h) in order to drive the reaction to completion. The solution was then diluted with ethyl acetate (80 mL), washed with saturated aqueous NH_4Cl, dried over Na_2SO_4, and concentrated. Purification by column chromatography (petroleum ether–ethyl acetate 9:1) afforded the corresponding methyl 2-(substituted phenyl)-4-hydroxyhexanoate or octanoate (yields in the range 44–69%), which was subjected to hydrolysis without further characterisation.

The above methyl ester (5.0 mmol) was dissolved in a mixture of MeOH–H_2O (3:1, 20 mL), and LiOH (6.5 mmol) was added to the solution. After 20 h at ambient temperature, the reaction mixture was cooled to 0 °C, and acidified with concd HCl to pH = 1. The mixture was heated to 40 °C for 30 min, diluted with ethyl acetate (20 mL), and washed with brine. The organic phase was dried over Na_2SO_4, and the solvent evaporated. Purification by column chromatography (petroleum ether–ethyl acetate 9:1) afforded the title γ-lactones (yields in the range 76–92%).

3-(4-Methylphenyl)-5-ethyltetrahydrofuran-2-one (6b). Colorless oil, yield 92%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.18–7.16 m, 4H, (Ar); 4.62–4.51 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 6.9$, $J_2 = 9.3$, (H3); 2.56–2.29 m overlapped, 2H, (H4); 2.34 s overlapped, 3H, (Ar–CH_3); 1.93–1.60 m, 2H, (–CH_2–), 1.04 t, 3H, $J = 7.4$, (–CH_3). **B**: 7.18–7.16 m, 4H, m, (Ar); 4.48–4.37 m, 1H, (H5); 3.85 dd, 1H, $J_1 = 8.5$, $J_2 = 12.7$, (H3); 2.78–2.67 m, 1H, (H4a); 2.34 s, 3H, (Ar–CH_3); 2.14–1.93 m, 1H, (H4b); 1.93–1.60 m, 2H, (–CH_2–); 1.05 t, 3H, $J = 7.4$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 177.47; 137.24; 134.16; 129.61; 127.43; 80.15; 45.30; 35.99; 28.41; 21.01; 9.64. **B**: 177.09; 137.28; 133.56; 129.49; 127.91; 79.75; 46.93; 37.60; 28.31; 21.05; 9.43. IR ($CDCl_3$): ν_{max} 1353, 1457, 1517, 1766, 2882, 2940, 2971 cm^{-1}. LRMS: *m*/*z* (%) 205 ($M^{\bullet+}$ + H, 100), 160 (43), 145 (7), 131 (60), 117 (17), 105 (7), 91 (13), 77 (2), 65 (5), 51 (3).

3-(4-Chlorophenyl)-5-ethyltetrahydrofuran-2-one (6h). Colorless oil, yield 86%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.36–7.31 m, 2H, (AA′BB′); 7.25–7.20 m, 2H, (AA′BB′); 4.61–4.51 m, 1H, (H5); 3.88 dd, 1H, $J_1 = 7.5$, $J_2 = 9.2$, (H3); 2.53–2.34 m, 2H, (H4); 1.92–1.63 m, 2H, (–CH_2–); 1.04 t, 3H, t, $J = 7.4$, (–CH_3). **B**: 7.36–7.31 m, 2H, (AA′BB′), 7.25–7.20 m, 2H, (AA′BB′); 4.50–4.38 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.80–2.69 m, 1H, (H4a); 2.07–1.92 m, 1H, (H4b); 1.92–1.63 m, 2H, (–CH_2–); 1.05 t, 3H, $J = 7.4$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.75; 135.54; 133.49; 129.08; 128.98; 80.11; 44.90; 35.67; 28.36; 9.63. **B**: 176.36; 134.95; 133.49; 129.41; 128.95; 79.82; 46.59; 37.40; 28.26; 9.42. IR ($CDCl_3$): ν_{max} 1353, 1463, 1494, 1768, 2881, 2940, 2970 cm^{-1}. LRMS: *m*/*z* (%) 225 ($M^{\bullet+}$, 43), 180 (72), 167 (11), 151 (100), 138 (75), 125 (12), 115 (65), 103 (50), 89 (12), 77 (22), 63 (12), 51 (15).

3-(3-Chlorophenyl)-5-ethyltetrahydrofuran-2-one (6i). Colorless oil, yield 89%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.31–7.26 m, 3H, (Ar); 7.21–7.15 m, 1H, (Ar); 4.62–4.51 m, 1H, (H5); 3.87 dd, 1H, $J_1 = 7.5$, $J_2 = 9.3$, (H3); 2.54–2.34 m, 2H, (H4); 1.92–1.61 m, 2H, (–CH_2–); 1.04 t, 3H, $J = 7.4$, (–CH_3). **B**: 7.31–7.26 m, 3H, (Ar); 7.21–7.15 m, 1H, (Ar); 4.49–4.37 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.80–2.69 m, 1H, (H4a); 2.08–1.92 m, 1H, (H4b); 1.92–1.61 m, 2H, (–CH_2–); 1.05 t, 3H, $J = 7.4$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.50; 139.01; 134.70; 130.17; 128.22; 127.80; 125.84; 80.15; 45.16; 35.56; 28.34; 9.59. **B**: 176.09; 138.41; 134.53; 130.03; 128.22; 127.76; 126.31; 79.84; 46.78; 37.29; 28.23; 9.40. IR ($CDCl_3$): ν_{max} 1353, 1432, 1464, 1480, 1575, 1599, 1773, 2882, 2940, 2971 cm^{-1}. LRMS: *m*/*z* (%) 225 ($M^{\bullet+}$, 100), 179 (12), 145 (8), 138 (32), 115 (18), 103 (12), 89 (4), 77 (1), 63 (3).

3-(3,4-Dichlorophenyl)-5-ethyltetrahydrofuran-2-one (6k). White crystals, yield 98%. Mp 66–67 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.45–7.38 m, 2H, (Ar); 7.18–7.12 m, 1H, (Ar); 4.62–4.52 m, 1H, (H5); 3.89–3.82 m, 1H, (H3); 2.53–2.35 m, 2H, (H4); 1.92–1.62 m, 2H, (–CH_2–); 1.04 t, 3H, $J = 7.4$, (–CH_3). **B**: 7.45–7.38 m, 2H, (Ar); 7.18–7.12 m, 1H, (Ar); 4.49–4.38 m, 1H, (H5); 3.85 dd, 1H, $J_1 = 8.6$, $J_2 = 12.9$, (H3); 2.81–2.70 m, 1H, (H4a); 2.06–1.92 m, 1H, (H4b); 1.92–1.62 m, 2H, (–CH_2–); 1.05 t, 3H, $J = 7.4$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.09; 137.09; 132.97; 131.81; 130.83; 129.69; 127.07; 80.10; 44.52; 35.33; 28.32; 9.60. **B**: 175.70; 136.51; 132.80; 131.81; 130.70; 130.06; 127.46; 79.88; 46.22; 37.09; 28.21; 9.40. IR ($CDCl_3$): ν_{max} 1353, 1474, 1563, 1772, 2882, 2940, 2971 cm^{-1}. LRMS: *m*/*z* (%) 259 ($M^{\bullet+}$, 19), 214 (78), 201 (4), 185 (38), 172 (100), 159 (9), 137 (37), 123 (7), 115 (30), 102 (40), 89 (4), 75 (11), 63 (8), 51 (9).

3-(4-Bromophenyl)-5-ethyltetrahydrofuran-2-one (6p). White crystals, yield 90%. Mp 45–46 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.61–4.51 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 9.2$, (H3); 2.52–2.34 m, 2H, (H4); 1.92–1.62 m, 2H, (–CH_2–); 1.04 t, 3H, $J = 7.4$, (–CH_3). **B**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.49–4.38 m, 1H, (H5); 3.85 dd, 1H, $J_1 = 8.5$, $J_2 = 12.9$, (H3); 2.80–2.69 m, 1H, (H4a); 2.06–1.92 m, 1H, (H4b); 1.92–1.62 m, 2H, (–CH_2–); 1.05 t, 3H, $J = 7.4$, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.65; 136.07; 132.05; 129.33; 121.57; 80.11; 44.97; 35.62; 28.36; 9.63. **B**: 176.26; 135.48; 131.91; 129.76; 121.62; 79.83; 46.66; 37.34; 28.26; 9.42. IR ($CDCl_3$): ν_{max} 1354, 1464, 1491, 1769, 2882, 2940, 2941 cm^{-1}. LRMS: *m*/*z* (%) 269 ($M^{\bullet+}$, 6), 224 (39), 211 (4), 195 (24), 184 (36), 169 (3), 145 (18), 128 (4), 116 (100), 103 (29), 89 (8), 77 (18), 63 (8), 57 (4), 51 (12).

3-(4-Chlorophenyl)-5-butyltetrahydrofuran-2-one (8h). White crystals, yield 76%. Mp 51–52 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.36–7.30 m, 2H, (AA′BB′); 7.25–7.19 m, 2H, (AA′BB′); 4.67–4.56 m, 1H, (H5); 3.88 dd, 1H, $J_1 = 7.5$, $J_2 = 9.2$, (H3); 2.53–2.33 m, 2H, (H4); 1.91–1.75 m, 1H, (–CHCH$_2$-a); 1.75–1.56 m, 1H, (–CHCH$_2$-b); 1.56–1.29 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$ Hz, (–CH$_3$). **B**: 7.36–7.30 m, 2H, (AA′BB′); 7.25–7.19 m, 2H, (AA′BB′); 4.54–4.43 m, 1H, (H5); 3.85 dd, 1H, $J_1 = 8.7$, $J_2 = 12.7$, (H3); 2.80–2.69 m, 1H, (H4a); 2.07–1.91 m, 1H, (H4b); 1.91–1.75 m, 1H, (–CHCH$_2$-a); 1.75–1.56 m, 1H, (–CHCH$_2$-b); 1.56–1.29 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.75 135.52; 133.48; 129.07; 128.98; 78.92; 44.87; 36.10; 35.06; 27.44; 22.38; 13.90. **B**: 176.37; 134.95; 133.48; 129.41; 128.94; 78.72; 46.59; 37.90; 34.98; 27.30; 22.41; 13.90. IR (KBr pellet): ν_{max} 1193, 1352, 1466, 1494, 1761, 2862, 2934, 2954 cm^{-1}. LRMS: *m*/*z* (%) 253 ($M^{\bullet+}$, 3), 208 (28), 191 (1), 167 (7), 151 (38), 138 (100), 125 (9), 115 (27), 103 (28), 89 (6), 77 (12), 63 (5), 51 (8).

3-(3-Chlorophenyl)-5-butyltetrahydrofuran-2-one (8i). Colorless oil, yield 79%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.33–7.24 m, 3H, (Ar); 7.21–7.15 m, 1H, (Ar); 4.68–4.58 m, 1H, (H5); 3.88 dd, 1H, $J_1 = 7.4$, $J_2 = 9.3$, (H3); 2.55–2.32 m, 2H, (H4); 1.95–1.72 m, 1H, (–CHCH$_2$-a); 1.72–1.55 m, 1H, (–CHCH$_2$-b); 1.55–1.26 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$, (–CH$_3$). **B**: 7.33–7.24 m, 3H, (Ar); 7.21–7.15 m, 1H, (Ar); 4.54–4.43 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 8.6$, $J_2 = 12.7$, (H3); 2.81–2.70 m, 1H, (H4a); 2.08–1.95 m, 1H, (H4b); 1.95–1.72 m, 1H, (–CHCH$_2$-a); 1.72–1.55 m, 1H, (–CHCH$_2$-b); 1.55–1.26 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.48; 138.99; 134.75; 130.18; 128.25; 127.84; 125.85; 78.97; 45.16; 36.05; 35.08; 27.43; 22.39; 13.90. **B**: 176.07; 138.41; 134.58; 130.04; 128.25; 127.78; 126.33; 78.73; 46.79; 37.82; 34.98; 27.30; 22.39; 13.90. IR ($CDCl_3$): ν_{max} 1353, 1432, 1467, 1479, 1574, 1599, 1769, 2862, 2933, 2959 cm^{-1}. LRMS: *m*/*z* (%) 253 ($M^{\bullet+}$, 37), 207 (13), 191 (1), 165 (4), 151 (6), 138 (100), 125 (5), 115 (21), 103 (21), 89 (4), 77 (2), 63 (3), 55 (3).

3-(3,4-Dichlorophenyl)-5-butyltetrahydrofuran-2-one (8k). Colorless oil, yield 86%. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.46–7.37 m, 2H, (Ar); 7.18–7.12 m, 1H, (Ar); 4.68–4.57 m, 1H, (H5), 3.86 dd, 1H, $J_1 = 7.9$, $J_2 = 9.1$, (H3); 2.54–2.34 m, 2H, (H4); 1.92–1.76 m, 1H, (–CHCH$_2$-a); 1.76–1.56 m, 1H, (–CHCH$_2$-b); 1.56–1.25 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.0$, (–CH$_3$). **B**: 7.46–7.37 m, 2H, (Ar); 7.18–7.12 m, 1H, (Ar); 4.55–4.44 m, 1H, (H5); 3.84 dd, 1H, $J_1 = 8.6$, $J_2 = 12.6$, (H3); 2.81–2.70 m, 1H, (H4a); 2.06–1.92 m, 1H, (H4b); 1.92–1.76 m, 1H, (–CHCH$_2$-a); 1.76–1.56 m, 1H, (–CHCH$_2$-b); 1.56–1.25 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.0$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.12; 137.06; 132.97; 131.82; 130.83; 129.70; 127.07; 78.93; 44.51; 35.79; 35.02; 27.41; 22.38; 13.89. **B**: 175.73; 136.49; 132.81; 131.82; 130.70; 130.07; 127.48; 78.78; 46.23; 37.61; 34.93; 27.29; 22.40; 13.89. IR ($CHCl_3$): ν_{max} 1352, 1473, 1563, 1770, 2874, 2934, 2960, 3027 cm^{-1}. LRMS: *m*/*z* (%) 287 ($M^{\bullet+}$, 27), 269 (1), 242 (23), 199 (2), 185 (4), 172 (100), 159 (5), 150 (14), 137 (9), 128 (5), 115 (13), 102 (18), 85 (3), 69 (1), 55 (4).

3-(4-Bromophenyl)-5-butyltetrahydrofuran-2-one (8p). White crystals, yield 89%. Mp 35–36 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ **A**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.67–4.56 m, 1H, (H5); 3.86 dd, 1H, $J_1 = 7.5$, $J_2 = 9.3$, (H3); 2.53–2.33 m, 2H, (H4); 1.92–1.76 m, 1H, (–CHCH$_2$-a); 1.76–1.59 m, 1H, (–CHCH$_2$-b); 1.59–1.30 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$, (–CH$_3$). **B**: 7.52–7.46 m, 2H, (AA′BB′); 7.20–7.14 m, 2H, (AA′BB′); 4.54–4.43 m, 1H, (H5); 3.84 dd, 1H, $J_1 = 8.6$, $J_2 = 12.6$, (H3); 2.80–2.69 m, 1H, (H4a); 2.07–1.92 m, 1H, (H4b); 1.92–1.76 m, 1H, (–CHCH$_2$-a); 1.76–1.59 m, 1H, (–CHCH$_2$-b); 1.59–1.30 m, 4H, (–CH$_2$CH$_2$–); 0.93 t, 3H, $J = 7.1$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ **A**: 176.67; 136.05; 132.04; 129.34; 121.57; 78.93; 44.95; 36.06; 35.06; 27.44; 22.39; 13.91. **B**: 176.28; 135.47; 131.91; 129.77; 121.61; 78.73; 46.66; 37.85; 34.99; 27.31; 22.42; 13.91. IR (KBr pellet): ν_{max} 1180, 1352, 1466, 1490, 1636, 1770, 2870, 2962 cm^{-1}. LRMS: *m*/*z* (%) 297 ($M^{\bullet+}$, 4), 252 (28), 211 (5), 195 (15), 184 (100), 171 (6), 141 (1), 129 (8), 116 (81), 103 (30), 89 (8), 77 (18), 63 (7), 51 (10).

Preparation of furanones 7b, h, i, k, p and 9h, i, k, p. Introduction of the double bond into the γ-lactone ring was carried out in the same manner as described above for the synthesis of furanones **5a–w**.

3-(4-Methylphenyl)-5-ethyl-2,5-dihydrofuran-2-one (7b). White crystals, yield 56%. Mp 53–54 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79–7.73 m, 2H, (AA′BB′); 7.50 d, 1H, $J = 1.9$, (H4); 7.25–7.19 m, 2H, (AA′BB′); 4.99 ddd, 1H, $J_1 = 1.9$, $J_2 = 5.8$, $J_3 = 6.8$, (H5); 2.37 s, 3H, (CH$_3$–Ar); 1.97–1.69 m, 2H, (–CH$_2$–); 1.06 t, 3H, $J = 7.4$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.90; 146.63; 139.34; 131.60; 129.29; 126.85; 126.71; 81.40; 26.72; 21.33; 9.18. IR ($CDCl_3$): ν_{max} 1337, 1457, 1513, 1751, 2881, 2925, 2939, 2973 cm^{-1}. LRMS: *m*/*z* (%) 203 ($M^{\bullet+}$ + H, 89), 185 (4), 173 (8), 159 (4), 145 (40), 128 (5), 117 (100), 102 (3), 91 (13), 77 (2), 63 (7), 51 (6). calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; found: C, 77.37; H, 7.18.

3-(4-Chlorophenyl)-5-ethyl-2,5-dihydrofuran-2-one (7h). White crystals, yield 64%. Mp 72–73 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.79 m, 2H, (AA′BB′); 7.56 d, 1H, $J = 1.9$, (H4); 7.41–7.36 m, 2H, (AA′BB′); 5.01 ddd, 1H, $J_1 = 1.9$, $J_2 = 5.7$, $J_3 = 6.8$, (H5); 1.98–1.72 m, 2H, (–CH$_2$–); 1.07 t, 3H, $J = 7.4$, (–CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.45; 147.81; 135.32; 130.75; 128.87; 128.31; 127.96; 81.53; 26.66; 9.20. IR ($CDCl_3$): ν_{max} 1338, 1407, 1492, 1755, 2881, 2939, 2973 cm^{-1}. LRMS: *m*/*z* (%) 222 ($M^{\bullet+}$ − H, 71), 207 (7), 193 (10), 165 (55), 159 (5), 137 (100), 129 (6), 115 (6), 102 (25), 87 (2), 75 (19), 63 (7), 57 (33), 51 (11). calcd for $C_{12}H_{11}ClO_2$: C, 64.73; H, 4.98; found: C, 64.80; H, 5.09.

3-(3-Chlorophenyl)-5-ethyl-2,5-dihydrofuran-2-one (7i). White crystals, yield 63%. Mp 45–46 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87–7.82 m, 1H, (Ar); 7.79–7.72 m, 1H, (Ar); 7.59 d, 1H, J = 1.7, (H4); 7.38–7.30 m, 2H, (Ar); 5.01 ddd, 1H, J_1 = 1.7, J_2 = 5.8, J_3 = 6.7, (H5); 1.97–1.70 m, 2H, (–CH_2–); 1.06 t, 3H, J = 7.4, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.21; 148.72; 134.59; 131.18; 130.61; 129.89; 129.30; 127.03; 125.11; 81.54; 26.59; 9.15. IR ($CDCl_3$): ν_{max} 1338, 1420, 1475, 1567, 1595, 1755, 2881, 2940, 2973 cm^{-1}. LRMS: m/z (%) 223 ($M^{\bullet+}$, 100), 205 (6), 193 (8), 177 (3), 165 (46), 159 (5), 137 (53), 130 (8), 115 (6), 102 (37), 87 (2), 75 (12), 63 (6), 57 (28), 51 (8). calcd for $C_{12}H_{11}ClO_2$: C, 64.73; H, 4.98; found: C, 64.79; H, 5.13.

3-(3,4-Dichlorophenyl)-5-ethyl-2,5-dihydrofuran-2-one (7k). White crystals, yield 71%. Mp 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 d, 1H, J = 2.0, (Ar); 7.73 dd, 1H, J_1 = 2.0, J_2 = 8.4, (Ar), 7.60 d, 1H, J = 1.9, (H4); 7.48 d, 1H, J = 8.4, (Ar); 5.02 ddd, 1H, J_1 = 1.9, J_2 = 5.7, J_3 = 6.8, (H5); 1.98–1.71 m, 2H, (–CH_2–); 1.07 t, 3H, J = 7.4, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.00; 148.78; 133.48; 132.95; 130.62; 129.78; 129.36; 128.82; 126.20; 81.61; 26.61; 9.20. IR ($CDCl_3$): ν_{max} 1337, 1472, 1553, 1756, 2881, 2940, 2974 cm^{-1}. LRMS: m/z (%) 256 ($M^{\bullet+}$–H, 80), 227 (9), 207 (48), 199 (44), 193 (10), 171 (81), 164 (10), 149 (5), 136 (41), 115 (6), 99 (19), 85 (5), 75 (15), 63 (8), 57 (100), 50 (12). calcd for $C_{12}H_{10}Cl_2O_2$: C, 56.06; H, 3.92; found: C, 55.90; H, 4.02.

3-(4-Bromophenyl)-5-ethyl-2,5-dihydrofuran-2-one (7p). White crystals, yield 58%. Mp 64–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77–7.72 m, 2H, (AA′BB′); 7.57 d, 1H, J = 1.9, (H4); 7.56–7.51 m, 2H, (AA′BB′); 5.00 ddd, 1H, J_1 = 1.9, J_2 = 5.7, J_3 = 6.9, (H5); 1.95–1.71 m, 2H, (–CH_2–); 1.06 t, 3H, J = 7.4, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.38; 147.91; 131.82; 130.80; 128.55; 128.40; 123.62; 81.55; 26.63; 9.20. IR ($CDCl_3$): ν_{max} 1288, 1337, 1403, 1462, 1488, 1589, 1755, 2881, 2939, 2973 cm^{-1}. LRMS: m/z (%) 223 (100), 205 (6), 193 (6), 177 (2), 165 (43), 159 (5), 137 (47), 130 (6), 115 (6), 102 (31), 87 (2), 75 (11), 63 (5), 57 (26), 51 (8). calcd for $C_{12}H_{11}BrO_2$: C, 53.96; H, 4.15; found: C, 53.80; H, 4.26.

3-(4-Chlorophenyl)-5-butyl-2,5-dihydrofuran-2-one (9h). White crystals, yield 53%. Mp 53–54 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.78 m, 2H, (AA′BB′); 7.56 d, 1H, J = 1.9, (H4); 7.41–7.35 m, 2H, (AA′BB′); 5.04 ddd, 1H, J_1 = 1.9, J_2 = 5.5, J_3 = 7.4, (H5); 1.89–1.66 m, 2H, (–CH<u>CH_2</u>–); 1.56–1.31 m, 4H, (–CH_2CH_2–); 0.93 t, 3H, J = 7.2, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.47; 148.19; 135.29; 130.46; 128.86; 128.29; 127.97; 80.59; 33.19; 27.14; 22.43; 13.85. IR (KBr pellet): ν_{max} 1143, 1336, 1466, 1493, 1632, 1749, 2855, 2929, 2960, 3069 cm^{-1}. LRMS: m/z (%) 250 ($M^{\bullet+}$-H, 100), 233 (7), 222 (4), 208 (6), 193 (12), 180 (8), 165 (48), 151 (7), 137 (83), 125 (8), 115 (13), 102 (53), 85 (82), 75 (18), 63 (7), 57 (78), 51 (13). calcd for $C_{14}H_{15}ClO_2$: C, 67.07; H, 6.03; found: C, 67.36; H, 6.34.

3-(3-Chlorophenyl)-5-butyl-2,5-dihydrofuran-2-one (9i). White crystals, yield 56%. Mp 39–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86–7.83 m, 1H, (Ar); 7.79–7.74 m, 1H, (Ar); 7.59 d, 1H, J = 1.9, (H4); 7.37–7.33 m, 2H, (Ar); 5.06 ddd, 1H, J_1 = 1.9, J_2 = 5.5, J_3 = 7.4, (H5); 1.90–1.62 m, 2H, (–CH<u>CH_2</u>–); 1.55–1.31 m, 4H, (–CH_2CH_2–); 0.93 t, 3H, J = 7.1, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.23; 149.03; 134.63; 131.22; 130.41; 129.92; 129.33; 127.05; 125.13; 80.60; 33.15; 27.11; 22.43; 13.85. IR (KBr pellet): ν_{max} 1124, 1338, 1476, 1566, 1595, 1636, 1754, 2871, 2932, 2957, 3073 cm^{-1}. LRMS: m/z (%) 250 ($M^{\bullet+}$–H, 94), 233 (8), 221 (3), 207 (31), 193 (13), 180 (14), 165 (33), 159 (11), 137 (75), 125 (7), 115 (14), 102 (58), 85 (100), 75 (21), 63 (8), 57 (81), 51 (14). calcd for $C_{14}H_{15}ClO_2$: C, 67.07; H, 6.03; found: C, 67.32; H, 6.20.

3-(3,4-Dichlorophenyl)-5-butyl-2,5-dihydrofuran-2-one (9k). White crystals, yield 54%. Mp 48–49 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 d, 1H, J = 2.0, (Ar); 7.73 dd, 1H, J_1 = 2.0, J_2 = 8.5, (Ar); 7.60 d, 1H, J = 1.9, (H4); 7.48 d, 1H, J = 8.5, (Ar); 5.06 ddd, 1H, J_1 = 1.9, J_2 = 5.5, J_3 = 7.4, (H5); 1.91–1.67 m, 2H, (–CH<u>CH_2</u>–); 1.54–1.32 m, 4H, (–CH_2CH_2–); 0.93 t, 3H, J = 7.1, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.03; 149.14; 133.47; 132.97; 130.63; 129.52; 129.39; 128.82; 126.20; 80.68; 33.12; 27.13; 22.42; 13.85. IR (KBr pellet): ν_{max} 1142, 1383, 1471, 1752, 2863, 2933, 2958, 3069 cm^{-1}. LRMS: m/z (%) 284 ($M^{\bullet+}$–H, 43), 267 (3), 253 (10), 242 (3), 227 (5), 207 (23), 199 (11), 171 (25), 149 (4), 136 (23), 115 (5), 99 (11), 85 (100), 75 (8), 63 (4), 57 (69), 51 (6). calcd for $C_{14}H_{14}Cl_2O_2$: C, 58.97; H, 4.95; found: C, 58.76; H, 5.11.

3-(4-Bromophenyl)-5-butyl-2,5-dihydrofuran-2-one (9p). White crystals, yield 54%. Mp 52–53 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77–7.72 m, 2H, (AA′BB′); 7.57 d, 1H, J = 1.9, (H4); 7.56–7.51 m, 2H, (AA′BB′); 5.03 ddd, 1H, J_1 = 1.9, J_2 = 5.5, J_3 = 7.4, (H5); 1.90–1.64 m, 2H, (–CH<u>CH_2</u>–); 1.56–1.31 m, 4H, (–CH_2CH_2–); 0.93 t, 3H, J = 7.1, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.40; 148.28; 131.83; 130.53; 128.54; 128.42; 123.60; 80.62; 33.16; 27.14; 22.43; 13.85. IR (KBr pellet): ν_{max} 1122, 1338, 1403, 1465, 1489, 1589, 1749, 2855, 2929, 2958, 3070 cm^{-1}. LRMS: m/z (%) 296 ($M^{\bullet+}$ +H, 85), 281 (2), 266 (4), 252 (11), 236 (9), 224 (6), 209 (35), 195 (3), 183 (70), 164 (5), 159 (6), 145 (7), 128 (10), 115 (13), 102 (98), 85 (97), 75 (26), 63 (9), 57 (100), 51 (18). calcd for $C_{14}H_{15}BrO_2$: C, 59.97; H, 5.12; found: C, 56.90; H, 5.26.

5-Ethyl-3-(3-pyridyl)-2,5-dihydrofuran-2-one (11). A solution of 3-iodopyridine (0.226 g, 1.1 mmol) in DMF (1 mL) was added to a suspension of Pd_2dba_3·$CHCl_3$ (0.021 g, 0.02 mmol), $AsPh_3$ (0.049 g, 0.16 mmol) and CuI (0.015 g, 0.08 mmol) in DMF (1 mL) under Ar. The resultant mixture was warmed to 50 °C, a solution of 5-ethyl-3-(tributylstannyl)-2,5-dihydrofuran-2-one (0.401 g, 1 mmol) in DMF (1.5 mL) was added, and the temperature was maintained at 50 °C for 6 h. A saturated

aqueous solution of KF was then added, the mixture stirred for 30 min, and then diluted with ethyl acetate. The resultant suspension was filtered, and the filtrate was washed with water, brine, and dried over Na_2SO_4. The solvent was removed, and the crude product purified by column chromatography (petroleum ether–ethyl acetate 7:3); yield 0.160 g (85%).

Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.99–8.93 m, 1H, (Ar2); 8.63–8.56 m, 1H, (Ar4); 8.30–8.24 m, 1H, (Ar6); 7.68 d, 1H, $J = 1.7$ Hz, (H4); 7.35 ddd, 1H, $J_1 = 8.0$ Hz, $J_2 = 4.9$ Hz, $J_3 = 0.6$ Hz, (Ar5); 5.09–5.02 m, 1H, (H5); 1.97–1.71 m, 2H, (–CH_2–); 1.06 t, 3H, $J = 7.4$ Hz, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.24, 149.95, 148.82, 147.94, 134.42, 129.20, 125.68, 123.45, 81.97, 26.57, 9.16. IR ($CDCl_3$): ν_{max} 2973, 2939, 1758, 1476, 1425, 1337 cm^{-1}. LRMS: 190 ($M^{\bullet+}$ + H, 82), 172 (2), 160 (7), 144 (5), 132 (23), 117 (14), 104 (100), 89 (3), 77 (17), 63 (7), 57 (11), 51 (21).

3,4-Dichlorophenyliodide. This compound was prepared from the commercially available 3,4-dichloroaniline by standard diazotation/iodination procedure. The physical and spectral data of the product were in accord with the literature.

Preparation of 12a and 12b by Pd-catalyzed cross-coupling. Solution I. A solution of iodobenzene (1.30 mmol) in dry THF (5 mL) under Ar was cooled to −78 °C. 1.6 M BuLi in hexanes (0.86 mL, 1.37 mmol) was added, and the mixture stirred for 20 min. A solution of dry $ZnBr_2$ (0.206 g, 0.91 mmol, flame-dried under high vacuum) in dry THF (5 mL) was added to the reaction mixture. The resultant mixture was slowly alloved to warm to room temperature, THF evaporated under vacuum, and the organozinc compound was redissolved in DMF (5 mL).

Solution II. A mixture of L_2PdCl_2 (0.05 mmol, L = PPh_3 for **12a**, tris(2-furyl)phosphine for **12b**) in dry THF (1 mL) was added to 1.6 M BuLi in hexanes (0.07 mL, 0.11 mmol) at −78 °C under Ar, and the resultant mixture was stirred for 1 h. A solution of 2-iodocyclopent-2-enone (0.208 g, 1.00 mmol) in dry DMF (4 mL) was then added, and the mixture was slowly allowed to warm to ambient temperature.

Solution I was added to solution II, and the reaction mixture was stirred for 5 h. The mixture was diluted with ethyl acetate, washed with water and saturated aqueous solution of NaCl, dried over Na_2SO_4, and concentrated. Purification by column chromatography (petroleum ether–EtOAc 98:2) afforded the pure products.

2-Phenylcyclopent-2-enone (12a). White crystals, yield 25%. Mp 68–70 °C, lit.[33] 71–72 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 t, 1H, $J = 2.9$ Hz, (H3), 7.73–7.64 m, 2H, (Ar); 7.43–7.29 m, 3H, (Ar); 2.73–2.66 m, 2H, (–CH_2–); 2.63–2.55 m, 2H, (–CH_2–). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.63, 159.02, 143.37, 131.58, 128.36, 128.28, 126.97, 35.72, 26.15. calcd for $C_{11}H_{10}O$: 83.51% C, 6.37% H; found 83.05% C, 6.58% H.

2-(4-Methylphenyl)cyclopent-2-enone (12b). White crystals, yield 33%. Mp 72–73 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78 t, 1H, $J = 2.9$ Hz, (H3); 7.63–7.56 m, 2H, (AA′BB′), 7.23–7.15 m, 2H, (AA′BB′); 2.73–2.66 m, 2H, (–CH_2–); 2.62–2.55 m, 2H, (–CH_2–); 2.36 s, 3H, (–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.80, 159.14, 143.24, 138.17, 129.06, 128.73, 126.84, 35.73, 26.09, 21.24. calcd for $C_{12}H_{12}O$: 83.69% C, 7.02% H; found: 83.89% C, 7.48% H.

Preparation of 12 c, h, k by Pd-catalyzed cross-coupling. Solution I. A solution of iodobenzene (1.30 mmol) in dry THF (5 mL) under Ar was cooled to −78 °C. 1.6 M BuLi in hexanes (0.86 mL, 1.37 mmol) was added, and the mixture stirred for 20 min. A solution of dry $ZnBr_2$ (0.206 g, 0.91 mmol, flame-dried under high vacuum) in dry THF (5 mL) was added to the reaction mixture. The resultant mixture was slowly allowed to warm to room temperature, THF evaporated under vacuum, and the organozinc compound was redissolved in DMF (5 mL).

Solution II. A suspension of $Pd_2dba_3{\cdot}CHCl_3$ (0.026 g, 0.025 mmol) and tris(2-furyl)phosphine (0.023 g, 0.10 mmol) in dry DMF (3 mL) was stirred under Ar at room temperature until it became a clear solution (10 min). A solution of 2-iodocyclopent-2-enone (0.208 g, 1.00 mmol) in dry DMF (2 mL) was then added.

Solution I was added to solution II, and the reaction mixture was stirred for 5 h. The mixture was diluted with ethyl acetate, washed with water and saturated aqueous solution of NaCl, dried over Na_2SO_4, and concentrated. Purification by column chromatography (petroleum ether–EtOAc 98:2) afforded the products.

Compound **12c** was obtained as a 2:1 mixture with 2-iodocyclopent-2-one; the mixture (0.065 g) was therefore dissolved in CH_3COOH (4 mL) and zinc powder (0.50 g) was added to the solution. The reaction mixture was stirred at room temperature for 48 h, and then poured into saturated aqueous Na_2CO_3 (15 mL). The product was extracted into EtOAc, the organic phase dried over Na_2SO_4, and the solvent removed. Pure cyclopentenone **12c** was obtained by column chromatography (petroleum ether–EtOAc 95:5).

2-(4-Methoxyphenyl)cyclopent-2-enone (12c). White crystals, yield 16%. Mp 104–106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 t, 1H, $J = 2.9$ Hz, (H3); 7.68–7.63 m, 2H, (AA′BB′); 6.94–6.87 m, 2H, (AA′BB′); 3.81 s, 3H, (–OCH_3); 2.71–2.65 m, 2H, (–CH_2–); 2.60–2.55 m, 2H, (–CH_2–). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.01, 159.63, 157.16, 142.72, 128.24, 124.23, 113.79, 55.24, 35.75, 26.03. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43; found: C, 76.25; H, 6.33.

2-(4-Chlorophenyl)cyclopent-2-enone (12h). White crystals, yield 32%. Mp 65–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 t, 1H, $J = 2.9$ Hz, (H3); 7.67–7.61 m, 2H, (AA′BB′); 7.37–7.31 m, 2H, (AA′BB′); 2.74–2.68 m, 2H, (–CH_2–); 2.62–2.57 m, 2H, (–CH_2–). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.34, 159.15, 142.25, 134.22, 130.00, 128.59, 128.28, 35.69, 26.20. calcd for $C_{11}H_9ClO$: C, 68.58; H, 4.71; found: C, 68.74H, 4.71.

2-(3,4-Dichlorophenyl)cyclopent-2-enone (12k). White crystals, yield 65%. Mp 91–93 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87 t, 1H, $J = 2.9$ Hz, (H3); 7.84 d, 1H, $J = 2.1$, (Ar2); 7.57 dd, 1H, $J_1 = 8.4$ Hz, $J_2 = 2.1$ Hz, (Ar6); 7.43 d, 1H, $J = 8.4$ Hz, (Ar5); 2.76–2.69 m, 2H, (–CH_2–); 2.64–2.57 m, 2H, (–CH_2–). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.83, 159.94, 141.17, 132.55, 132.33, 131.47, 130.35, 128.78, 126.23, 35.65, 26.25. IR ($CDCl_3$): ν_{max} 2923, 1703, 1552, 1472, 1439, 1404, 1315 cm^{-1}. LRMS: 226 ($M^{\bullet+}-H$, 100), 207 (4), 191 (6), 163 (95), 149 (7), 135 (10), 127 (54), 113 (6), 99 (12), 86 (8), 74 (25), 63 (26), 50 (27). calcd for $C_{11}H_8Cl_2O$: C, 58.18; H, 3.55; found: C, 58.53; H, 3.82.

Biology

In vitro antifungal activities of the compounds, ketoconazole (Janssen-Cilag), and amphotericin B (Sigma-Aldrich) were evaluated on a panel of one ATCC (*C. albicans* ATCC 44859) and seven clinical isolates of yeasts (*C. krusei* E28, *Candida tropicalis* 156, *Candida glabrata* 20/I, *Trichosporon beigelii* 1188), and filamentous fungi (*A. fumigatus* 231, *A. corymbifera* 272, *Trichophyton mentagrophytes* 445) from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. Quality control strains were involved. All the isolates were maintained on Sabouraud dextrose agar prior to being tested.

Minimum inhibitory concentrations (MICs) were determined by the microdilution format of the NCCLS M27-A guidelines.[11] Dimethyl sulfoxide (100%) served as a diluent for all compounds; the final concentration did not exceed 2%. RPMI 1640 (Sevapharma, Prague) medium supplemented with L-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 by 10 N NaOH was used as the test medium. The wells of the microdilution tray contained 100 μL of the RPMI 1640 medium with 2-fold serial dilutions of the compounds (125–0.24 μmol/l for the new compounds) and 100 μL of inoculum suspension. Fungal inoculum in RPMI 1640 was prepared to give a final concentration of $5 \times 10^3 \pm 0.2$ cfu mL^{-1}. The trays were incubated at 35 °C and MICs were read visually for filamentous fungi and photometrically for yeasts as an optical density (OD) at 540 nm after 24 and 48 h. The MIC values for the dermatophytic strain (*T. mentagrophytes*) were determined after 72 h and 120 h. The MICs were defined as 80% inhibition of the growth of control. MICs were determined twice and in duplicate. The deviations from the usually obtained values given in Tables 1 and 2 were no higher than the nearest concentration value up and down the dilution scale.

Acknowledgements

This research was supported by Charles University (project No. 259/2001) and the Ministry of Education of the Czech Republic (projects Nos. MSM 111600001 and 111600002).

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