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Regio- and stereochemical aspects in synthesis of 2-allyl derivatives of glycolic, mandelic and lactic acids and their iodocyclisations to 3-hydroxy-3,4-dihydrofuran-2(5*H*)-ones

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Abstract—Glyoxalic, phenylglyoxalic and pyruvic acids **1a–c** undergo regio- and diastereoselective indium mediated allylations with allyl and cinnamyl bromides and ethyl 4-bromocrotonate to provide respective 2-allyl-, 2-(1-phenylallyl)- and 2-[(1-ethoxycarbonyl)allyl]-derivatives of glycolic, mandelic and lactic acids **3–11**. The reactions follow Cram's chelation model for allylation and give *syn* addition products as the major or the only products. Diastereoselective iodocyclisations of **3–8** and **10** provide 3-hydroxy-3,4-dihydrofuran-2(5*H*)-ones (**15–21**), the stereochemical outcome, of which depends on the nature and position of the substituents on the substrate, choice of solvent and base. The relative stereochemistries have been ascertained by X-ray structure and NOE experiments and coupling constants in the ^{1}H NMR spectra.
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1. Introduction

2(5*H*)-Furanones have attained considerable significance as the synthetic targets due to their wide-spread biological activity, occurrence in nature and their use as synthetic intermediates.[1] Approaches towards stereoselective synthesis are therefore a continued challenge in their synthesis. The electrophile induced intramolecular cyclisation of an appropriately substituted alkene ester constitutes one practical approach for their synthesis.[2]

The availability of the appropriate alkene esters or acid moieties constitutes the key step in the synthesis of target furanones. The allylation of 2-oxocarboxylic acids could be a simple and general approach for the synthesis of functionalized alkene acids.[3–5] However, the earlier reported procedures for the allylation under Grignard type conditions with allyl boronates[3] and allyl trichloromethyl silane[4] or under Barbier type conditions by using mixed metal combinations $BiCl_3$–Mg(0)/$BiCl_3$–Zn(0)[5] suffer from pre-synthesis of the reagents and non-availability of substituted allyl organometallic reagents. In recent years, indium mediated allylations have provided simple synthetic procedures for the aqueous media allylation of carbonyl compounds even in the presence of proton donor functionalities.[6] The presence of hydroxy-, alkoxy or amino moieties at α- or β- to carbonyl group has led to considerable π-facial discrimination through participation of Cram's chelation model.[7–9] However, the participation of COOH coordination in indium mediated allylation is not known.

Now we report that 2-oxocarboxylic acids **1a–1c** undergo regio- and stereoselective indium mediated allylations with allyl and cinnamyl bromides and ethy 4-bromoccrotonate to provide respective 2-allyl-, 2-(1-phenylallyl)- and 2-[(1-ethoxycarbonyl)allyl]- derivatives of glycolic, mandelic and lactic acids **3–11**.[10] These allylation reactions, in general, follow Cram's cyclic model to provide *syn* addition products as the only or the major products. 2-Hydroxypent-4-en-1-oic acids **3–8** and **10**, depending on the nature and position of the substituents on the substrate, choice of solvent and base undergo diastereoselective iodocyclisations to provide a general procedure for 3-hydroxy-3,4-dihydrofuran-2(5*H*)-ones **15–21**. It has been observed that the balance of steric factors on C-2 and C-3 position of respective alkenoic acids significantly affects the outcome of stereoselectivities in 3-hydroxy-3,4-dihydrofuran-2(5*H*)-ones.

2. Results and discussion

2.1. Allylation of 2-oxocarboxylic acids

A solution of glyoxalic acid **1a**, allyl bromide **2a** and indium

Keywords: Indium allylation; Diastereoselective; Iodocyclisations; Furan-2-ones.
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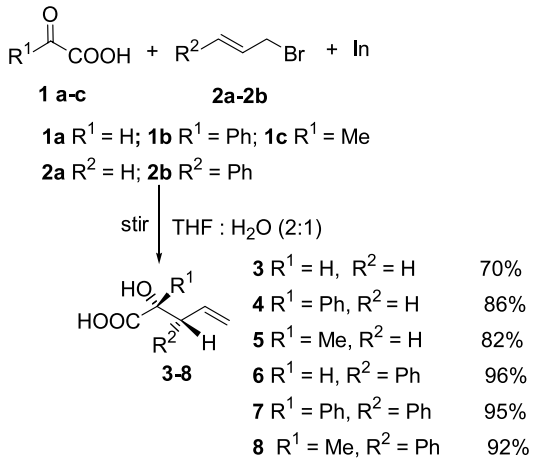


Scheme 1.

metal (suspension) (1:1.5:1) in THF–H_2O (2:1) on stirring at 0 °C, following usual work-up and chromatography gave 2-allyl glycolic acid **3**, as a pale yellow liquid (70%), M^+ *m/z* 116 (Scheme 1). Similarly, phenylglyoxalic acid **1b** and pyruvic acid **1c** underwent indium mediated allylation with allyl bromide to give respective 2-allyl- mandelic and lactic acids **4** and **5** (82–86%).

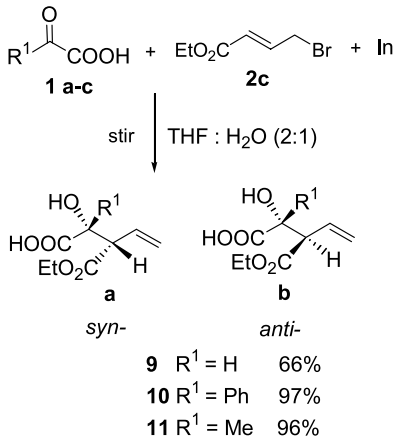
In order to extend the scope of this reaction to achieve a diasteroselective allylation, the reactions of **1a–c** have been performed with cinnamyl bromide and ethyl 4-bromocrotonate. Glyoxalic acid **1a** on indium mediated allylation with cinnamyl bromide **2b** gave 2-(1-phenylallyl) glycolic acid **6**, pale yellow liquid (96%), M^+ *m/z* 192, 116 ($M^+ - C_6H_5$) (Scheme 1). In its ^1H NMR spectrum, the presence of 1H double doublet at δ 3.86 due to C*H*Ph and lack of CH_2 signals in the region δ 2.0–3.5 confirmed the formation of γ- addition product. The presence of only one set of signals in both ^1H and ^{13}C NMR spectra points to a single diastereomer being formed.

Similarly, indium mediated allylation of **1b** and **1c** with cinnamyl bromide gave the respective 2-(1-phenylallyl)-mandelic and pyruvic acids **7** and **8** (Table 1). Therefore, 2-oxocarboxylic acids **1a–c** undergo indium mediated highly γ-regio- and diastereoselective Barbier type allylation with cinnamyl bromide. The stereochemistries as *syn* addition products to 2-allyl carboxylic acids **6–8** have been assigned on the basis of the X-ray crystal structure of iodocyclised products **19a** and **19b** and coupling constant and NOE experiments on the ^1H NMR spectra of **18–20** (Scheme 1).

Table 1. Reactions of 2-oxocarboxylic acids **1a–c** with **2b** and **2c**

S.no.	R^1	R^2	Product	Yield (%)	dr (*syn*: *anti*)
1	H	C_6H_5	**6**	96	>99:1
2	C_6H_5	C_6H_5	**7**	95	>99:1
3	CH_3	C_6H_5	**8**	92	>99:1
4	H	$CO_2C_2H_5$	**9**	66	86:14
5	C_6H_5	$CO_2C_2H_5$	**10**	97	90:10[a]
6	CH_3	$CO_2C_2H_5$	**11**	96	86:14

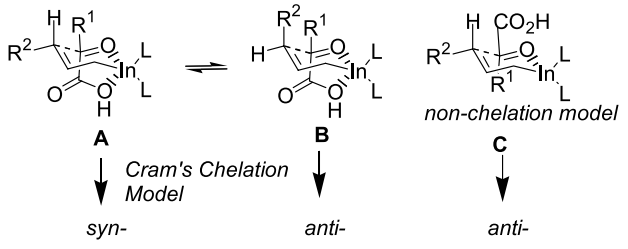
[a] After single crystallization increases to >98:2.



Scheme 2.

Similarly, **1b** and **1c** underwent indium mediated allylation with **2c** to provide respective 2-[(1-ethoxy carbonyl)allyl] mandelic and lactic acids **10** and **11** (Scheme 2). Both **10** and **11** have been formed as a mixture of *syn* and *anti* diastereomers, the *syn* diastereomer being the major product (Table 1). In the case of **10**, the diastereomeric ratio could be increased to >98:2 by single crystallization. Therefore, allylation of **1a–c** with ethyl 4-bromocrotonate leads to lower diastero-selectivities than those found with cinnamyl bromide.

The formation of *syn* addition products as the only, or major products, in allylation of **1a–c** with **2b** and **2c** could be explained by the participation of Cram's chelation model A (Scheme 3) where the conformation of 2-oxocarboxylic acid is locked by complexation with allylindium reagent and allylic anion adds from the sterically less hindered face. In case of ethyl 4-bromocrotonate, the lower diastereoselectivities, could be due to partial participation of transition state B or non-chelation model C (Scheme 3).[11,12]

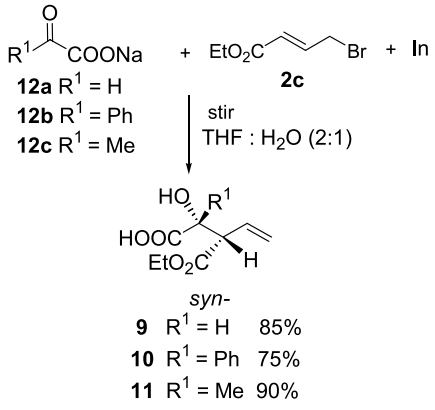


Scheme 3.

We envisioned that the increased ease of participation of carboxylic acid moiety in forming cyclic transition state with allylindium reagent could increase the participation of Cram's chelation model and thus the diastereoselectivity. The conversion of carboxylic acid to carboxylate anion (**12a–c**), due to the presence of negative charge, would facilitate chelation during the allyl transfer process. Alternatively, the conversion of acid to amide **13**, due to delocalisation of the nitrogen lone pair of electrons with carbonyl, is expected to increase the participation of amide oxygen towards complexation with indium and thus higher diastereoselectivities.

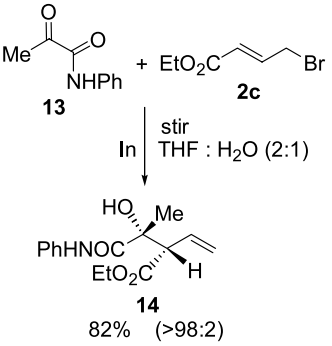
However, sodium pyruvate **12c** did not undergo allylation with ethyl 4-bromocrotonate in THF–H_2O. On performing

the reaction at pH 4.7±0.2, the allylation proceeded quite smoothly and in a highly diastereoselective manner to provide **11** (dr>98:2), but the yield of **11** was lowered to 50%. On using 2 equiv of indium metal and 3 equiv of **2c**, the yield of **11** could be increased to 90%. During the reaction, the pH of the solution was maintained by adding 4 N NaOH solution from time to time. Similarly, **12a** and **12b** underwent diastereoselective allylation with **2c** at pH 4.7±0.2 to provide **9** and **10**, respectively, in dr> 98:2 (Scheme 4). The allylation of **12a–c** was completed in shorter times (4–6 h) than the time taken for the reactions of respective 2-oxocarboxylic acids **1a–c** (18–24 h). Both higher diastereoselectivities and shorter reaction time for allylation at pH 4.7±0.2 could be assigned to better participation of the carboxylate anion in chelation than the carboxylic acid moiety. In an alternative approach, the pH of the solution of **1a–c** in THF–H_2O (2:1) was adjusted to 6±0.2 by adding NaOH solution and then ethyl 4-bromocrotonate and indium was added and the stirring was continued. The reactions were completed in 4–6 h and **9–11** were formed with diastereoselectivities >98:2.



Scheme 4.

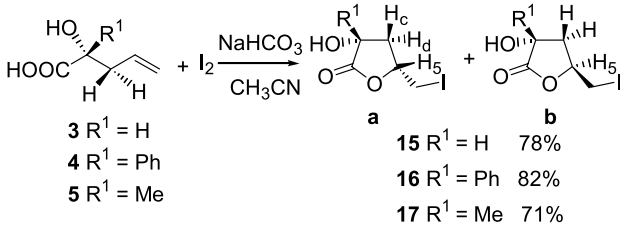
Similarly, indium mediated allylation of **13**, with ethyl 4-bromocrotonate in THF–H_2O proceeded quite smoothly (4–5 h) and in a highly diastereoselective manner (dr> 98:2) to provide **14** (Scheme 5). Both higher diastereoselectivities and shorter reaction time for allylation point to the increased participation of amide oxygen towards complexation with indium.



Scheme 5.

2.2. Synthesis of 3-hydroxy-3,4-dihydrofuran-2(5*H*)-ones (15–21)

A solution of **3** in dry CH_3CN containing I_2 and suspended $NaHCO_3$ (3 equiv) on stirring at 0 °C after work-up gave **15a**, mp 69 °C, M^+ *m/z* 242 in diastereomeric ratio >99:1 (Scheme 6). The ^1H NMR spectrum of **15a** exhibits five 1H signals with well defined multiplicities and one 1H signal as multiplet and shows that each proton is magnetically non-equivalent. The decoupling of 1H multiplet at δ 4.41–4.45 coverts dt at δ 1.98 to triplet, and ddd's at δ 2.89 to double doublet, two dd's at δ 3.31 and 3.45 to doublets and has been assigned the 5-H proton. The decoupling of the dd at δ 4.62 (H_3) modulates dt at δ 1.98, and doublet of dd at δ 2.89 and confirms the signals at δ 1.98 and 2.89 due to ring CH_2 protons. The higher coupling constants (J=10.4 Hz) between H-c, and H-5 with signal at δ 1.98 and lower coupling constants (J=5.4/8.6 Hz) with signal at δ 2.89 support the stereochemistries defined in Figure 1. The positive NOE of signal H_c (δ 2.89) with H_3 and H_5 signals and lack of NOE of H_d with these protons conspicuously assigns these stereochemistries. Therefore **3** undergoes highly diastereoselective iodocyclisation to provide (3*R**,5*R**)-3-hydroxy-5-iodomethylfuran-2(5*H*)-one (**15a**).



Scheme 6.

2-Allylmandelic acid **4** on iodocyclisation (I_2–CH_3CN–$NaHCO_3$) provided the crude reaction mixture, which in its ^1H NMR spectrum shows two multiplets at δ 4.33–4.41 (1H) and 4.68–4.79 (1H) due to CH in 66:34 ratio and pointed it to be a mixture of two diastereomeric furan-2(5*H*)-ones **16a** and **16b**. However, even on repeated chromatography and crystallization, the two components could not be separated. Since the diastereoselectivity in iodocyclisation reactions is significantly affected by the choice of solvent and base, the iodocyclisation of **4** was attempted under various conditions by using solvents of varied polarities and Na^+/RNH_4^+ carboxylates in place of COOH (Table 2).

On performing the reaction of **4** in dry THF, the dr **16a/16b** was increased to 80:20, which was further increased to 91:9 on carrying out the reaction in dry DMF. The sodium salt of

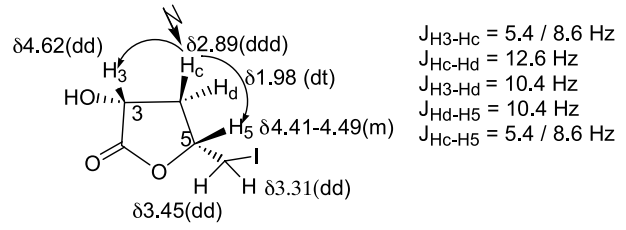


Figure 1. The relative stereochemistries in **15a** from NOE and coupling constant experiments.

Table 2. Disatereoselectivities in iodocyclisations of **4**

S. no.	Base	Solvent	Time (h)	dr	Yield %
Effect of solvent					
1	$NaHCO_3$	CH_3CN	72	66:34	82
2	$NaHCO_3$	THF	6	80:20	83
3	$NaHCO_3$	DMF	1–2	91:9	56
Effect of base					
4	Benzyl amine	THF	3–5	86:14	63
5	[a]	THF	3–5	89:11	90
6	[a]	DMF	1–2	93:7	56
7	[b]	THF	3–5	91: 9	82
8	[b]	DMF	1–2	95: 5	70
9	Pyrrolidine	THF	3–5	90:10	62

[a] Phenylethylamine.
[b] Diisopropylamine.

4 in dry DMF also gave **16a** and **16b** in 91:9 ratio but failed to react in THF or CH_3CN, probably due to its poor solubility in latter solvents. It seems that on moving from THF and CH_3CN, to DMF, the nature of the nucleophile shifts from carboxylic acid to carboxylate ion. Since ammonium salts find more solubility in non-polar solvents, the reactions of **4** were performed in the presence of various amines. The iodocyclisation of **4** in I_2-benzylamine/phenyl ethyl amine by using THF as solvent gave **16a/16b** in dr 86:14–89:11 (Table 2, s. no. 4,5), which was further increased to 90:10–91:9 by using secondary alkyl amines as base (s. no. 7, 9). On performing iodocyclisation of **4** in the presence of primary and secondary amines and by using DMF as solvent, the dr **16a/16b** was enhanced to 93:7 and 95:5 (s. no. 6, 8), respectively. The 95:5 mixture of **16a/16b** on crystallization gave pure **16a**, mp 70 °C, M^+ *m/z* 318.

Compound **16a**. in its ^1H NMR spectrum shows four 1H double doublets and one 1H multiplet along with aromatic (5*H*) protons. The decoupling of multiplet at δ 4.33–4.41 converts all the four double doublets to doublets and unambiguously assigns H-5 proton to this multiplet. In its ^1H-^{13}C COSY spectrum, the correlation of most up-field negative carbon (CH_2I) signal at δ 5.13 (due to iodine effect) with two double doublets at δ 3.34 and 3.47 assigns them to be CH_2I protons. The irradiation of 1H multiplet at δ 4.33–4.41 (H-5) enhances the signals for H_c (δ 2.87) and phenyl protons by 7.6 and 13.6%, respectively, (Fig. 2) and points to the presence of H-5, H_c and 3-Ph moieties on the same face of furan-2(5*H*)-one ring. The higher coupling constant between H-5 and H_d ($J=10$ Hz) than between H-5 and H_c ($J=5.4$ Hz) (Fig. 2) also supports the presence of H_d proton trans to H-5 proton. This data confirms the structure (3*S**,5*R**)-3-hydroxy-3-phenyl-5-iodomethylfuran-2(5*H*)-one (**16a**) to this compound.

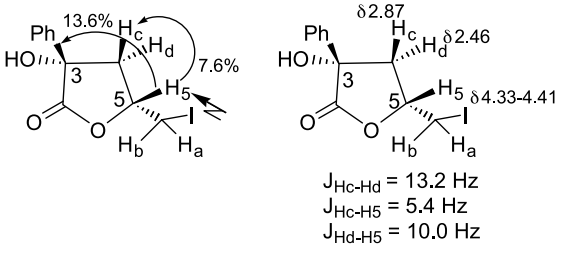
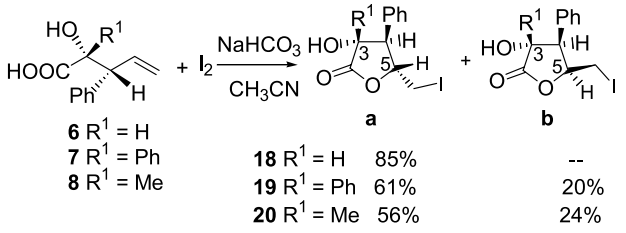


Figure 2. The relative stereochemistries in **16a** from NOE and coupling constant experiments.

The signals for the minor component **16b** were picked from the 2:1 mixture of **16a** and **16b**. The irradiation of H-5 signal at δ 4.68–4.79 does not show NOE with the phenyl protons and has been assigned the structure **16b**.

2-Allyl lactic acid **5** on iodocyclisation provided 80:20 mixture of two diastereomers, which on column chromatography followed by repeated crystallization resulted in isolation of major diastereomer **17a**. The assignment of the signals to each proton and carbon has been made on the basis of ^1H, ^{13}C NMR, decoupling experiments and ^1H–^{13}C COSY spectra. The relative stereochemistries at C-3 and C-5 carbons have been ascertained from NOE experiment. The irradiation of H-5 multiplet at δ 4.44–4.49 shows positive NOE for CH_3 (12.6%) and H_c (δ 2.54) (5.2%). These observations show that H-4, CH_3 and H-5 are on the same side of furan-2(5*H*)-one ring and have been assigned the structure (3*R**,5*R**)-3-hydroxy-3-methyl-5-iodomethyl-furan-2(5*H*)-one (**17a**).

2-(1-Phenylallyl)glycolic acid **6** on iodocyclisation gave only one diastereomer **18a** (85%), mp 84 °C, M^+ *m/z* 318 (Scheme 7). The $J=10.2$ Hz coupling constant between H-5 (δ 4.25–4.31) and H-4 (δ 3.42) and $J=10.2$ Hz coupling constant between H-3 (δ 4.77) and H-4 (δ 3.42) assign *trans*, *trans* stereochemistry between H-3, H-4 and H-5. The irradiation of H-3 doublet at δ 4.77 shows NOE enhancement of H-5 (3.7%) and Ph (6.1%) protons and irradiation of H-5 multiplet (δ 4.25–4.31) shows NOE enhancement of H-3 (2.2%) and Ph (5.7%) protons and confirms the structure (3*R**,4*R**,5*R**)-3-hydroxy-4-phenyl-5-iodomethyl-furan-2 (5*H*)-one (**18a**) for this compound.



Scheme 7.

2-(1-Phenylallyl)mandelic acid **7** on iodocyclisation in CH_3CN–$NaHCO_3$ gave 75:25 mixture of two diastereomers **19a** (61%) and **19b** (20%). On using DMF–$NaHCO_3$ the diastereoselectivity decreased to 50:50. In ^1H NMR spectrum of major component $J_{H\text{-}4,\ H\text{-}5}=10.4$ Hz shows the presence of H-4 and H-5 on the opposite side of furan-2(5*H*)-one ring (**19a**). The minor component in its ^1H NMR spectrum exhibits $J_{H\text{-}4,\ H\text{-}5}=5.4$ Hz and points to the presence of H-4 and H-5 protons on the same side of furan-2(5*H*)-one ring (**19b**). However, the relative stereochemsitries at C-3 and C-4 in **19a** and **19b** could not be assigned on the basis of NMR or NOE experiments and have been confirmed by X-ray structure analysis.

The X-ray crystal structures of both **19a** (Fig. 3) and **19b** (Fig. 4), show the presence of two aryl rings on the same face of furan-2(5*H*)-one ring and confirm the formation of *syn* homoallylic alcohol **7**. In **19a**, the CH_2I and OH

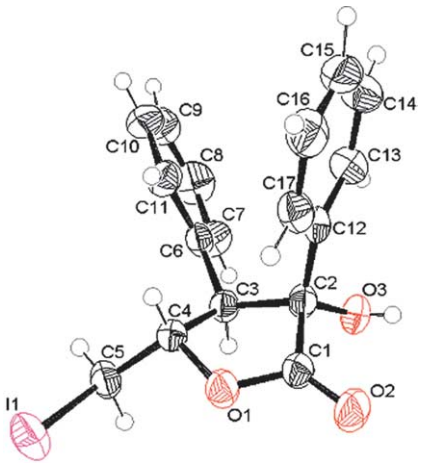


Figure 3. The ORTEP view (50% ellipsoide) of **19a**.

moieties are on the same face. This results in placement of H-3 and H-4 protons on the opposite face of furan-2(5*H*)-one ring and is in agreement with $J_{H\text{-}4,\,5}=10.4$ Hz observed in its ^{1}H NMR spectrum. Similarly, in the case of **19b**, $J_{H\text{-}4,5}=5.4$ Hz is in agreement with placement of H-3 and H-4 protons on the same side of furan-2(5*H*)-one ring as confimed by X-ray structure. In both **19a** and **19b** C(4)–O(1)–C(1)–C(2) make one mean plane (Tables 3 and 4) and C-3 carbon moves out of plane by an angle of $23\pm1°$. The two phenyl rings on C-2 and C-3 carbons are placed at dihedral angle of 44.6(3)° in **19a** and 39.2(3)° in **19b**. The placement of CH_2I unit in two different orientations in **19a** and **19b** controls the placement of C-2 and C-3 phenyl rings. In the case of **19a**, 3-phenyl ring is placed at equatorial position [C(6)–C(3)–C(4)–O(1) –163.5(2)°] and 2-phenyl is placed at axial position [O(1)–C(1)–C(2)–C(12) 97.3(3)°]. But in the case of **19b**, 2-phenyl ring is placed at equatorial position [O(1)–C(1)–C(2)–C(12) −151.4(2)°] and 3-phenyl is placed at axial position [C(6)–C(3)–C(4)–O(1) 86.9(3)°].

Iodine mediated intramolecular cyclisation of **8** in CH_3CN provided 70:30 mixture of **20a** and **20b**. In the case of **20a** the irradiation of H-5 multiplet (δ 4.57–4.64) shows NOE enhancement of CH_3 (22.6%) and phenyl (21.8%) protons. Therefore, H-5, CH_3 and phenyl are on the same side of furan-2(5*H*)-one ring and confirms the structure (3*R**,4*R**,5*R**)-3-hydroxy-3-methyl-4-phenyl-5-iodo methyl-furan-2(5*H*)-one (**20a**). In the case of **20b**,

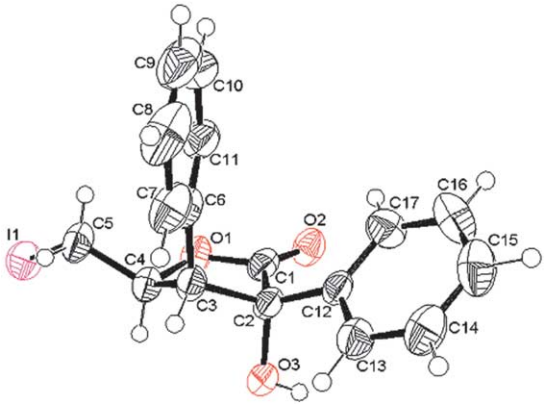
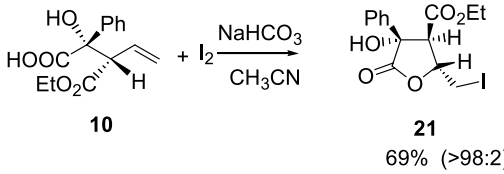


Figure 4. The ORTEP view (50% ellipsoide) of **19b**.

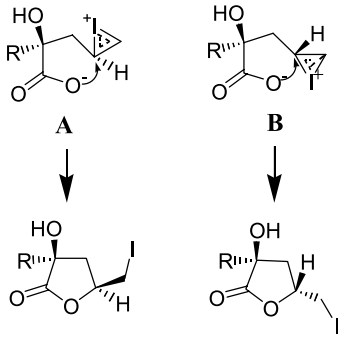
$J_{H4,5}=4.8$ Hz shows the presence of H-4 and H-5 protons on the same side of furan-2(5*H*)-one ring and lack of NOE of H-5 with phenyl and methyl protons points the placement of methyl and phenyl groups on the opposite face than H-5 and confirms structure (3*R**,4*R**,5*S**)-3-methyl-4-phenyl-3-hydroxy-5-idomethyl-furan-2(5*H*)-one (**20b**) to the minor product.

Compound **10** underwent diastereoselective iodocyclisation to provide **21** in dr>98:2 (Scheme 8). The assignment of signals has been made on the basis of ^{1}H NMR and ^{1}H decoupling experiments. The coupling constant $J=9$ Hz between H-4 (d, δ 3.62) and H-5 (m, δ 4.64–4.69), shows the presence of H-4 and H-5 protons on the opposite side of furan-2(5*H*)-one ring. The irradiation of H-5 multiplet shows positive NOE for phenyl ring multiplet (5.0%) and $COOCH_2$ multiplet (7.67%) and points to the presence of phenyl ring, COOEt and H-5 moieties on the same side of furan-2(5*H*)-one ring. Therefore, iodine mediated cyclisation of **10** gives only (3*S**,4*S**, 5*R**)-3-hydroxy-4-ethoxycarbonyl-5-iodomethylfuran-2(5*H*)-one **21**.



Scheme 8.

The formation of two diastereomers of furan-2(5*H*)-ones could be visualized to proceed through intermediates **A** and **B** (Scheme 9) formed by the addition of iodine on either of the two faces of double bond. Iodonium ion intermediate **A** would result in the formation of 3,5-substituted product with OH and CH_2I groups placed *syn* to each other, while iodonium ion intermediate **B** would result in formation of product with OH and CH_2I groups on the opposite faces of furane ring. The present iodine mediated intramolecular cyclisations of 2-hydroxy-4-pentene-1-oic acid and its derivatives result in formation of the products with OH and CH_2I moieties present on same side either exclusively or predominantly and involve the preferential participation of intermediate **A**. This preference arises probably due to stabilisation of iodonium ion intermediate by its electrostatic interactions with lone pair of oxygen in intermediate **A**. Such participation of oxygen lone pairs in the



Scheme 9.

stabilization of iodonium ion has earlier been suggested in iodocyclizations of 4-hydroxy-pentenoic acids.[13]

3. Conclusions

Thus, 2-oxocarboxylic acids undergo facile indium mediated allylation in aqueous media with allyl bromide, cinnamyl bromide and ethyl 4-bromocrotonate to provide the corresponding 2-allyl derivatives of glycolic, mandelic and lactic acids. In the case of reactions with cinnamyl bromide and ethyl 4-bromocrotonate, the allylation reactions proceed with high γ-regio- and diastereoselectivities. The formation of *syn* addition products confirms possible chelation of carboxylic acid moiety with indium during allyl transfer process. The iodine mediated intramolecular cyclizations of **3–8** and **10** provide furan-2(5*H*)-one derivatives with OH and CH_2I moieties placed *syn* to each other as the major or the only product.

4. Experimental

4.1. General details

Melting points were determined in capillaries and are uncorrected. ^{1}H NMR spectra were recorded on JEOL Al 300 MHz instrument using $CDCl_3$ solution containing tetramethylsilane as an internal standard. The chemical shifts are reported in δ values relative to TMS and coupling constants (J) are expressed in Hz. ^{13}C NMR spectra were recorded at 75 MHz and values are reported relative to $CDCl_3$ signal at δ 77.0. Chromatography was performed with silica 100–200 mesh and the reactions were monitored by thin-layer chromatography (TLC) with glass plates coated with silca gel HF-254.

4.2. General procedure

Procedure A. The 2-oxocarboxylic acid **1** (5 mmol), allyl bromide (7.5 mmol) and indium metal (fine flakes) (5 mmol) were taken in THF–H_2O (2:1) mixture and the reaction mixture was stirred in an ice bath until the indium metal dissolved (18–24 h). The turbid reaction mixture was treated with 4 N HCl and extracted with $CHCl_3$. The organic solvent was distilled off and the residue was column chromatographed (silica gel, 60–120 mesh) to isolate the allyl addition product.

Procedure B. The sodium salt of 2-oxocarboxylic acid **1** (5 mmol), **2c** (15 mmol) and indium metal (fine falkes) (10 mmol) were taken in THF–H_2O (2:1) mixture. The pH 4.7 of the reaction was controlled initially by addition of acetic acid. The reaction mixture was stirred in an ice bath until the indium metal dissolved. During the course of reaction the pH was controlled 4.7 ± 0.2 by the addition of aqueous NaOH (4 N). After completion of the reaction, the turbid reaction mixture was treated with 4 N HCl and extracted with $CHCl_3$.The organic solvent was distilled off and the residue was column chromatographed (silica gel, 60–120 mesh) to isolate the allyl addition product.

4.2.1. 2-Allylglycolic acid (3). *Procedure A*. 406 mg, 70%; pale yellow liquid; FAB mass M^+ *m/z* 116 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.34–2.63 (m, 2H, CH_2), 4.22–4.32 (m, 1H, CH), 4.60–4.92 (b, 1H, OH, exchanges with D_2O), 5.04–5.17 (m, 2H, $=CH_2$), 5.62–5.85 (m, 1H, =CH), 6.24–6.55 (bs, 1H, OH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 38.47 (−ve, CH_2), 69.65 (+ve, CH), 118.07 (+ve, CH), 132.93 (−ve, CH_2), 176.23 (ab, C); IR ν_{max} (neat): 1722 (C=O), 3440 (OH) cm^{-1}. (For Na salt: mp > 300 °C. Found: C, 43.2; H, 5.1. $C_5H_7O_3Na$ requires C, 43.48; H, 5.07%).

4.2.2. 2-Allylmandelic acid (4). *Procedure A*. White solid 825 mg, 86%; mp 110 °C ($CHCl_3$); FAB mass M^+ *m/z* 192 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 1H, OH, exchanges with D_2O), 2.71 (dd, $J_1=13.8$ Hz, $J_2=6.8$ Hz, 1H of CH_2), 2.96 (dd $J_1=13.8$ Hz, $J_2=6.8$ Hz, 1H of CH_2), 5.11–5.22 (m, 2H, $=CH_2$), 5.69–5.89 (m, 1H, =CH), 7.19–7.64 (m, 5*H*, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 44.32 (−ve, CH_2), 78.08 (ab, C), 119.72 (−ve, CH_2), 125.67 (+ve, CH), 127.89 (+ve, CH), 128.45 (+ve, CH), 133.78 (+ve, CH), 140.85 (ab, C), 178.79 (ab, C); IR ν_{max} (neat): 1720 (C=O), 3442 (OH) cm^{-1}. Found C, 61.4; H, 5.3%. $C_{11}H_{11}O_3Na$ requires C, 61.68; H, 5.14%.

4.2.3. 2-Allyllactic acid (5). *Procedure A*. 533 mg, 82%; colourless liquid; FAB mass M^+ *m/z* 130 (M^+), 111 (M^+ − allyl); ^{1}H NMR ($CDCl_3$): δ 1.49 (s, 3H, CH_3), 2.41 (dd, 1H, $J_1=10$ Hz, $J_2=6$ Hz, 1H of CH_2), 2.57 (dd, 1H, $J_1=10$ Hz, $J_2=6$ Hz, 1H of CH_2), 5.16–5.29 (m, 2H, $=CH_2$), 5.74–5.87 (m, 1H, =CH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 25.22 (−ve, CH_2), 44.51 (+ve, CH_3), 74.41 (ab, C), 119.33 (+ve, CH), 131.79 (−ve, CH_2), 180.18 (ab, C); IR ν_{max} (neat): 1724 (C=O), 3446 (OH) cm^{-1}. (For Na salt: mp > 300 °C. Found: C, 47.3; H, 5.7. $C_6H_{10}O_3Na$ requires C, 47.36; H, 5.92%).

4.2.4. (2*R,3*R**)-2-(1-Phenylallyl)-glycolic acid (6).** *Procedure A*. 920 mg, 96%; light yellow liquid; FAB mass M^+ *m/z* 192 (M^+), 116 ($M^+ - C_6H_5$); ^{1}H NMR ($CDCl_3$): δ 2.18 (s, 1H, OH, exchanges with D_2O), 3.86 (dd, $J_1=7.6$ Hz, $J_2=4$ Hz, 1H, CH), 4.59 (d, $J=4$ Hz, 1H, CH), 5.20–5.29 (m, 2H, $=CH_2$), 6.25 (ddd, $J_1=17.4$ Hz, $J_2=10$ Hz, $J_3=7.4$ Hz, 1H, =CH), 7.22–7.37 (m, 5*H*, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 52.82 (+ve, CH), 73.74 (+ve, CH), 117.29 (−ve, CH_2), 127.37 (+ve, CH), 128.46 (+ve, CH), 128.74 (+ve, CH), 137.72 (ab, C), 136.88 (+ve, CH), 177.72 (ab, C); IR ν_{max} (neat): 1687 (C=O), 3521 (OH) cm^{-1}. (For Na salt: mp > 300 °C. Found C, 61.4; H, 5.3%. $C_{11}H_{11}O_3Na$ requires C, 61.68; H, 5.14%).

4.2.5. (2*R,3*R**)-2-(1-Phenylallyl)-mandelic acid (7).** *Procedure A*. White solid 206 g, 95%; mp 168 °C (CH_2Cl_2); FAB mass M^+ *m/z* 269 ($M^+ + 1$); ^{1}H NMR ($CDCl_3$): δ 4.39 (s, 1H, OH, exchanges with D_2O), 4.40 (d, $J=9.6$ Hz, 1H, CH), 4.79–4.99 (m, 2H, $=CH_2$), 5.96 (ddd, $J_1=17.4$ Hz, $J_2=9.6$ Hz, $J_3=8.1$ Hz, 1H, =CH), 7.19–7.41 (m, 8H, ArH), 7.72–7.73 (m, 2H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 57.13 (+ve, CH), 80.75 (ab, C), 118.49 (−ve, CH_2), 126.42 (+ve, CH), 127.26 (+ve, CH), 127.89 (+ve, CH), 128.12 (+ve, CH), 128.21(+ve, CH), 129.43 (+ve, CH), 135.29 (+ve, CH), 138.93 (ab, C), 139.17 (ab, C), 177.75 (ab, C); IR ν_{max}

(KBr): 1685 (C=O), 3519 (OH) cm^{-1}. (Found C, 76.3; H, 5.9. $C_{17}H_{16}O_3$ requires C, 76.12; H, 5.97%).

4.2.6. (2*R,3*R**)-2-(1-Phenylallyl)-lactic acid (8).** *Procedure A*. 948 mg, 92%; light yellow liquid; FAB mass M^+ *m/z* 206 (M^+); ^1H NMR ($CDCl_3$): δ 1.49 (s,3H, CH_3), 3.55 (d, $J=9.6$ Hz, 1H, CH), 5.16–5.31 (m, 2H, $=CH_2$), 6.26 (dt, $J_1=16.8$ Hz, $J_2=9.6$ Hz, 1H, =CH), 7.24–7.29 (m, 5*H*, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 24.42 (+ve, CH_3), 57.61 (+ve, CH), 76.77 (ab, C), 118.80 (−ve, CH_2), 127.19 (+ve, CH), 128.38 (+ve, CH), 128.53 (+ve, CH), 135.39 (+ve, CH), 139.39 (ab, C), 180.41 (ab, C); IR ν_{max} (neat): 1728 (C=O), 3481 (OH) cm^{-1}. (For Na salt: mp > 300 °C. Found C, 63.1; H, 6.1. $C_{12}H_{13}O_3Na$ requires C, 63.16; H, 5.70%).

4.2.7. (2*R,3*S**)-2-[(1-Ethoxy carbonyl)allyl] glycolic acid (9).** *Procedure B*. 798 mg, 85%; light yellow liquid; FAB mass M^+ *m/z* 188 (M^+), 143 (M^+-COOH); ^1H NMR ($CDCl_3$): δ 1.31 (t, $J=7$ Hz, 3H, CH_3), 2.09 (s, 1H,OH, exchanges with D_2O), 3.62 (dd, $J_1=8.4$ Hz, $J_2=3.6$ Hz, 1H, CH), 4.20 (s, 1H, OH, exchanges with D_2O), 4.22 (q, $J=7$ Hz, 2H, OCH_2), 4.47 (d, $J=3.6$ Hz,1H, CH), 5.26–5.38 (m, 2H, $=CH_2$), 5.92 (dt, $J_1=17.4$ Hz, $J_2=8.4$ Hz, 1H, =CH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 14.21 (+ve, CH_3), 50.21 (+ve, CH), 60.32 (−ve, CH_2), 71.20 (+ve, CH), 121.23 (−ve, CH_2), 136.13 (+ve, CH), 173.22 (ab, C), 175.59 (ab, C); IR ν_{max} (neat): 1728 (C=O), 3481 (OH) cm^{-1}. (For Na salt: mp > 300 °C. Found C, 45.4; H, 4.9. $C_8H_{11}O_5Na$ requires C, 45.71; H, 5.24%).

4.2.8. (2*S,3*S**)-2-[(1-Ethoxy carbonyl)allyl] mandelic acid (10).** *Procedure B*. White solid 991 mg, 75%; mp 97–98 °C (CH_2Cl_2); FAB mass M^+ *m/z* 219 (M^+-COOH); ^1H NMR ($CDCl_3$): δ 1.29 (t, $J=7.2$ Hz, 3H, CH_3), 2.20 (s, 1H, OH, exchanges with D_2O), 4.14 (d, $J=8.2$ Hz, 1H, CH), 4.22 (q, $J=7.2$ Hz, 2H, OCH_2), 5.02–5.17 (m, 2H, $=CH_2$), 5.56–5.62 (ddd, $J_1=17.4$ Hz, $J_2=7.2$ Hz, $J_3=6.4$ Hz, 1H, =CH), 7.29–7.42 (m, 8H, ArH), 7.58–7.63 (m, 2H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 13.90 (+ve, CH_3), 56.88 (+ve, CH), 61.31 (−ve, CH_2), 78.73 (ab, C), 120.64(−ve, CH_2), 125.66 (+ve, CH), 127.66 (+ve, CH), 128.01 (+ve, CH), 130.23 (+ve, CH), 138.51 (ab, C), 173.22 (ab, C), 175.63 (ab, C); IR ν_{max} (KBr): 1706 (C=O), 1730 (C=O), 3504 (OH) cm^{-1}. (Found: C, 63.3; H, 6.0. $C_{14}H_{16}O_5$ requires C, 63.63; H, 6.06%).

4.2.9. (2*R,3*S**)-2-[(1-Ethoxy carbonyl)allyl] lactic acids (11).** *Procedure B*. 909 mg, 90%; light yellow liquid; FAB mass M^+ *m/z* 202 (M^+); ^1H NMR ($CDCl_3$): δ 1.33 (t, $J=8$ Hz, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.84 (br s, 1H, OH, exchanges with D_2O), 4.17 (dd, $J_1=8.4$ Hz, $J_2=3.6$ Hz, 1H, CH), 4.20 (s, 1H, OH, exchanges with D_2O), 4.22 (q, $J=7$ Hz, 2H, OCH_2), 5.31–5.44 (m, 2H, $=CH_2$), 5.89 (ddd, $J_1=17$ Hz, $J_2=9$ Hz, $J_3=8.4$ Hz, 1H, =CH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 12.91 (+ve, CH_3), 22.87 (+ve, CH_3), 55.96 (+ve, CH), 59.54 (−ve, CH_2), 73.18 (ab, C), 119.46 (−ve, CH_2), 130.59 (+ve, CH), 176.96 (ab, C), 176.23 (ab, C); IR ν_{max}: 1730 (C=O), 1785 (C=O), 3558 (OH) cm^{-1}. (For Na salt of **11**: mp > 300 °C. Found: C, 48.0; H, 6.1. $C_9H_{13}NaO_5$ requires C, 48.21; H, 5.8%).

4.3. Synthesis of 2-oxo-*N*-phenyl-propionamide (13)

The mixture of ethyl lactate (1 mmol, 2 g) and aniline (1 mmol, 1.6 g) was heated without solvent for 5–6 h on water bath. The progress of the reaction was monitored by TLC. On completion of reaction (TLC) the reaction mixture was diluted with 10 ml of water and extracted with $CHCl_3$ (3×20 ml). The organic phase was washed with water and dried over sodium sulphate. The removal of solvent provided yellow liquid. The crude reaction mixture was column chramotaographed over silica gel to isolate pure 2-hydroxy-*N*-phenylpropionamide (2.23 g, 80%). It was treated with Jones reagent. On completion the reaction mixture was diluted with 10 ml of water and extracted with $CHCl_3$ (3×20 ml). The organic phase was washed with water and dried over sodium sulphate. The crude reaction mixture was column chromatographed over silica gel to isolate pure (**13**) (1.14 g, 52%);white solid, mp 62 °C ($CHCl_3$); FAB mass M^+ *m/z* 163 (M^+); ^1H NMR ($CDCl_3$): δ 2.55 (s, 3H, CH_3), 7.16 (t, $J=7.4$ Hz, 1H, ArH), 7.35 (t, $J=7.4$ Hz, 2H, ArH), 7.62 (d, $J=9$ Hz, 2H, ArH), 8.70 (br s, 1H, NH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 24.40 (+ve, CH_3), 119.68 (+ve, CH), 125.26 (+ve, CH), 129.20 (+ve, CH), 136.21 (ab, C), 162.56 (ab, C), 197.29 (ab, C); IR ν_{max} (KBr): 1674 (C=O), 1710 (C=O), 3321 (NH) cm^{-1}. (Found: C, 66.2; H, 5.3; N, 8.3. $C_9H_9NO_2$ requires C, 66.3; H, 5.52; N, 8.59%).

4.3.1. (2*R,3*S**)-2-[(1-Ethoxy carbonyl)allyl]-*N*-phenyl-propionamide (14).** *Procedure A*. White solid 1.135 g, 82%; mp 71 °C ($CHCl_3$); FAB mass M^+ *m/z* 277 (M^+); ^1H NMR ($CDCl_3$): δ 1.23 (t, $J=7.2$ Hz, 3H, CH_3), 1.37 (s, 3H, CH_3), 3.83 (d, $J=9.2$ Hz, 1H, CH), 4.09–4.22 (m, 2H, OCH_2), 4.95 (s, 1H, OH, exchanges with D_2O), 5.35–5.44 (m, 2H, $=CH_2$), 5.90 (ddd, $J_1=17.2$ Hz, $J_2=10.8$ Hz, $J_3=9.2$ Hz, 1H, =CH) 7.13 (t, $J=7.2$ Hz, 1H, ArH), 7.35 (t, $J=7.5$ Hz, 2H, ArH), 7.55 (d, $J=9$ Hz, 2H, ArH), 8.73 (br s, 1H, NH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 14.03 (+ve, CH_3), 24.01 (+ve, CH_3), 54.20 (+ve, CH), 61.65 (−ve, CH_2), 76.73 (ab, C), 119.59 (+ve, CH), 122.16 (−ve, CH_2), 124.36 (+ve, CH), 128.95 (+ve, CH), 130.15 (+ve, CH), 137.11 (ab, C), 173.81 (ab, C), 175.13 (ab, C); IR ν_{max} (KBr): 1668 (C=O), 1701 (C=O), 3355 (NH), 3421 (OH) cm^{-1}. (Found: C, 64.8; H, 7.1; N, 4.9. $C_{15}H_{19}NO_4$ requires C, 64.98; H, 6.86; N, 5.05%).

4.4. Iodine mediated cyclization of homoallylic alcohols

Procedure C. Sodium hydrogen carbonate (0.009 mol) was added to an ice cold solution of homoallylic alcohol (0.003 mol) in dry acetonitrile and resulting suspension was stirred for 15 min at 0 °C. Iodine (0.009 mol) was added and stirring was continued for 24–72 h at 0 °C in dark (TLC monitoring). The reaction mixture was diluted with water and extracted with $CHCl_3$. The organic layer was washed with saturated aqueous sodium thiosulphate to remove excess of iodine. The organic layer was dried over anhydrous sodium sulphate and was distilled off. The residue was column chromatographed (silica gel 100–200) to isolate substituted furan-2(5*H*)-one derivatives.

Procedure D. Di-isopropylamine (0.009 mol) was added to an ice cold solution of homoallylic alcohol (0.003 mol) in

dry DMF and resulting solution was stirred for 15 min at 0 °C. Iodine (0.009 mol) was added and stirring was continued for 24 h at 0 °C in dark (TLC monitoring). The reaction mixture was diluted with water and extracted with ether. The organic layer was washed with saturated aqueous sodium thiosulphate to remove excess of iodine. The organic layer was dried over anhydrous sodium sulphate and was distilled off. The residue was column chromatographed (silica gel 100–200) to isolate substituted furan-2(5*H*)-one derivatives.

4.4.1. (3*R,5*R**)-3-Hydroxy-5-iodomethylfuran-2(5*H*)-one (15a).** *Procedure C*. White solid 566 mg, 78%; mp 69 °C (benzene); FAB mass M^+ *m/z* 242 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.98 (dt, $J_1=12.6$ Hz, $J_2=10.4$ Hz, 1H of CH_2 [H_d]), 2.89 (ddd, $J_1=12.6$ Hz, $J_2=8.6$ Hz, $J_3=5.4$ Hz, 1H, 1H of CH_2 [H_c]), 3.31 (dd, $J_1=10.4$ Hz, $J_2=7.5$ Hz, 1H, 1H of ICH_2), 3.45 (dd, $J_1=10.4$ Hz, $J_2=5.4$ Hz, 1H, 1H of ICH_2), 3.82 (br s, 1H, OH, exchanges with D_2O), 4.41–4.45 (m, 1H, H_5), 4.62 (dd, $J_1=10.4$ Hz, $J_2=8.6$ Hz, 1H, H_3); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 5.41(−ve, CH_2I), 37.41 (−ve, CH_2-4), 68.84 (+ve, CH-3), 75.52 (+ve, CH-5), 176.53 (ab, C=O); IR ν_{max} (KBr): 1772 (C=O), 3361 (OH) cm^{-1}. (Found: C, 25.2; H, 2.9. $C_5H_7IO_3$ requires C, 24.79; H, 2.89%).

4.4.2. (3*S,5*R**)-3-Hydroxy-3-phenyl-5-iodomethylfuran-2(5*H*)-one(16a).** Procedure *D*. White solid 562 mg, 59%; mp 70 °C (benzene); FAB mass M^+ *m/z* 318 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.46 (dd, $J_1=13.2$ Hz, $J_2=10$ Hz,1H, 1H of CH_2 [H_d]), 2.87 (dd, $J_1=13.2$ Hz, $J_2=5.4$ Hz, 1H of CH_2 [H_c]), 3.11 (br s, 1H, OH, exchanges with D_2O), 3.34 (dd, $J_1=10.5$ Hz, $J_2=7.8$ Hz,1H, 1H of CH_2i), 3.47 (dd, $J_1=10.5$ Hz, $J_2=5.4$ Hz,1H, 1H of CH_2i), 4.33–4.41 (m,1H, H_5), 7.23–7.46 (m, 5*H*,Arh); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 5.13 (−ve, CH_2I), 44.64 (−ve, CH_2-4), 75.53 (+ve, CH-5), 79.12 (ab, C-3), 125.16 (+ve, CH), 129.09 (+ve, CH), 129.13 (+ve, CH), 139.55 (ab, C), 176.99 (ab, C=O); IR ν_{max} (KBr): 1778 (C=O), 3429 (OH) cm^{-1}. (Found: C, 41.8; H, 3.3. $C_{11}H_{11}IO_3$ requires C, 41.51; H, 3.46%).

4.4.3. (3*S,5*S**)-3-Hydroxy-3-phenyl-5-iodomethylfuran-2(5*H*)-one (16b).** From the spectrum of 1:2 mixture of **16a** and **16b** the lower concentration signals have been chosen. ^{1}H NMR ($CDCl_3$): δ 2.21 (dd, $J_1=18$ Hz, $J_2=8.2$ Hz, 1H, 1H of ring CH_2), 2. 83 (dd, $J_1=18$ Hz, $J_2=6$ Hz, 1H, 1H of ring CH_2), 3.29 (dd, $J_1=10$ Hz, $J_2=1.8$ Hz, 1H, 1H of CH_2I) and 3.45 (dd, $J_1=10$ Hz, $J_2=4.4$ Hz, 1H, 1H of CH_2I), 4.68–4.79 (m, 1H, H_5), 7.23–7.46 (m, 5*H*, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 7.78 (−ve, CH_2), 45.87 (−ve, CH_2), 76.11 (+ve, CH), 78.79 (ab, C), 125.55 (+ve, CH), 128.46 (+ve, CH), 139.65 (ab, C), 176.21 (ab, C).

4.4.4. (3*R,5*R**)-3-Hydroxy-3-methyl-5-iodomethylfuran-2(5*H*)-one (17a).** *Procedure C*. White solid 430 mg, 56%; mp 95 °C (benzene); FAB mass M^+ *m/z* 256 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.52 (s, 3H, CH_3), 2.18 (dd, $J_1=13.2$ Hz, $J_2=8.4$ Hz, 1H, 1H of CH_2 [H_d]), 2.54 (dd, $J_1=13.2$ Hz, $J_2=10.8$ Hz, 1H, 1H of CH_2 [H_c]), 2.61 (br s, 1H, OH, exchanges with D_2O), 3.32 (dd, $J_1=10.4$ Hz, $J_2=8.1$ Hz, 1H, 1H of CH_2i), 3.46 (dd, $J_1=10.4$ Hz, $J_2=4.8$ Hz, 1H, 1H of CH_2i), 4.44–4.49 (m, 1H, H_5); Decoupling: the decoupling of H_5 multiplet at δ 4.44–4.49, converts two dd δ 3.32 and δ 3.46 (CH_2I) and at δ 2.18 (H_d) and 2.54 (H_c) into doublets NOE experiments: the irradiation of H_5 multiplet at δ 4.44–4.49 shows positive NOE for CH_3 (12.6%) and H_c (δ 2.54) (5.2%); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 5.65 (−ve, CH_2I), 24.647 (+ve, CH_3), 42.82 (−ve, CH_2-4), 73.93 (ab, C-3), 75.82 (+ve, CH-5), 178.44 (ab, C=O); IR ν_{max} (KBr): 1762 (C=O), 3442 (OH) cm^{-1}. (Found: C, 28.4; H, 3.6. $C_6H_9IO_3$ requires C, 28.13; H, 3.52%).

4.4.5. (3*R,4*R**,5*R**)-3-Hydroxy-4-phenyl-5-iodomethylfuran-2(5*H*)-one (18a).** *Procedure C*. White solid 810 mg, 85%; mp 84 °C (benzene); FAB mass M^+ *m/z* 318 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.04 (br s, 1H, OH, exchanges with D_2O), 3.27 (dd, $J_1=11.4$ Hz, $J_2=5.4$ Hz, 1H, 1H of CH_2I), 3.42 (t, $J=10.4$ Hz, 1H, H_4), 3.52 (dd, $J_1=11.4$ Hz, $J_2=3.3$ Hz, 1H, 1H of CH_2i), 4.25–4.31 (m, 1H, H_5), 4.77 (d, $J=10.4$ Hz, 1H, H_3), 7.28–7.45 (m, 5*H*, Arh); Decoupling of 1H multiplet at δ 4.25–4.31 changes two double doublets at δ 3.27, 3.52 into doublets and triplet at δ 3.42 into doublet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 4.77(−ve, CH_2I), 55.65 (+ve, CH), 74.16 (+ve, CH), 79.75 (+ve, CH), 127.72 (+ve, CH), 128.52 (+ve, CH), 129.33 (+ve, CH), 134.48 (ab, C), 175.02 (ab, C); IR ν_{max} (KBr): 1791 (C=O), 3384 (OH) cm^{-1}. (Found: C, 41.2; H, 3.6. $C_{11}H_{11}IO_3$ requires C, 41.51; H, 3.46%).

4.4.6. (3*S,4*R**,5*R**)-3-Hydroxy-3-phenyl-4-phenyl-5-iodomethyl-furan-2(5*H*)-one (19a).** *Procedure C*. White solid 721 mg, 61%; mp 203 °C; FAB mass M^+ *m/z* 394 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.71 (br s, 1H, OH, exchanges with D_2O), 3.27 (dd, $J_1=12.0$ Hz, $J_2=6.0$ Hz, 1H, 1H of CH_2I), 3.53 (dd, $J_1=12.0$ Hz, $J_2=4.0$ Hz, 1H, 1H of CH_2i), 3.79 (d, $J=10.6$ Hz, H_4), 4.40–4.49 (m, 1H, H_5), 6.66–6.71 (m, 2H, Arh), 6.71–6.95 (m, 2H, Arh), 7.13–7.26 (m, 2H, Arh); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 4.43 (−ve, CH_2), 59.96 (+ve, CH), 77.42 (+ve, CH), 82.17 (absent, C), 127.13 (+ve, CH), 127.71 (+ve, CH), 127.77 (+ve, CH), 128.21 (+ve, CH), 128.37 (+ve, CH), 129.47 (+ve, CH), 131.94 (ab, C), 136.17 (ab, C),176.62 (ab, C); IR ν_{max} (KBr): 1760 (C=O), 3377 (OH) cm^{-1}. (Found: C, 51.5; H, 3.6%. $C_{17}H_{15}IO_3$ requires C, 51.78; H, 3.81%).

4.4.7. (3*S,4*R**,5*S*)-3-Hydroxy-3-phenyl-4-phenyl-5-iodomethyl-furan-2(5*H*)-one (19b).** *Procedure C*. White solid 235 mg, 20%; mp 257 °C (benzene); FAB mass M^+ *m/z* 394 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.91 (t, $J=9.6$ Hz, 1H of CH_2I), 3.51 (br s, 1H, OH, exchanges with D_2O), 3.38 (dd, $J_1=9.6$ Hz, $J_2=6.3$ Hz, 1H, 1H of CH_2i), 3.90 (d, $J=5.4$ Hz, H_4), 5.41–5.47 (m, 1H, H_5), 6.90–7.92 (m, 2H, Arh), 7.02–7.11 (m, 2H, Arh), 7.34–7.36 (m, 6H, Arh); Decoupling: the decoupling of H_5 multiplet at δ 5.41–5.47, converts triplet at δ 2.91, dd at δ 3.55 into doublet and doublet at δ 3.61 into singlet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 0.79 (−ve, CH_2), 57.24 (+ve, CH), 58.92 (+ve, CH), 80.82 (+ve, CH), 81.83 (ab, C), 127.12 (+ve, CH), 127.77 (+ve, CH), 128.21 (+ve, CH), 128.37 (+ve, CH), 129.47 (+ve, CH), 132.32 (ab, C), 132.65 (ab, C), 176.58 (ab, C); IR ν_{max} (KBr): 1775 (C=O), 3438 (OH) cm^{-1}. (Found: C, 52.1; H, 3.6. $C_{17}H_{15}IO_3$ requires C, 51.78; H, 3.81%).

4.4.8. (3*R,4*R**,5*R**)-3-Hydroxy-3-methyl-4-phenyl-5-iodomethyl-furan-2(5*H*)-one (20a).** *Procedure C*. White

solid 558 mg, 56%; mp 134 °C (benzene); FAB mass M^+ *m/z* 332 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.59 (s, 3H, CH_3), 2.82 (s, 1H, OH, exchanges with D_2O), 3.34 (dd, $J_1=11.4$ Hz, $J_2=6.0$ Hz, 1H, 1H of CH_2I), 3.53–3.66 (m, 2H, 1H of CH_2i and H_4), 4.57–4.64 (m, 1H, H_5), 7.22–7.26 (m, 2H, Arh), 7.33–7.44 (m, 3H, Arh); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 4.80 (−ve, CH_2I), 21.06 (+ve, CH_3), 57.62 (+ve, CH-4), 78.08 (+ve, CH-5), 81.12 (ab, C), 128.271 (+ve, CH), 128.38 (+ve, CH), 128.99 (+ve, CH), 129.05 (+ve, CH), 129.29 (+ve, CH),132.91 (ab, C), 177.47 (ab, C); IR ν_{max} (KBr): 1764 (C═O), 3365 (OH) cm^{-1}. (Found: C, 43.7; H, 4.2. $C_{12}H_{13}IO_3$ requires C, 43.37; H, 3.92%).

4.4.9. (3*R,4*R**,5*S**)-3-Hydroxy-3-methyl-4-phenyl-5-iodomethyl-furan-2(5*H*)-one (20b).** *Procedure C*. White solid 231 mg, 24%; mp 145 °C (benzene); FAB mass M^+ *m/z* 322 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.20 (s, 3H, CH_3), 2.37 (br s, 1H, OH, exchanges with D_2O), 2.82 (t, $J=9.6$ Hz, 1H, 1H of CH_2I), 3.33 (dd, $J_1=9.6$ Hz, $J_2=6.0$ Hz, 1H, 1H of CH_2i), 3.61 (d, $J=4.8$ Hz, 1H, H_4), 5.29–5.36 (m, 1H, H_5), 7.07–7.12 (m, 2H, Arh), 7.31–7.76 (m, 3H, ArH); *Decoupling*: the decoupling of H_5 multiplet at δ 5.29–5.34, converts two dd's at δ 2.82, δ 3.55 into doublet and doublet at δ 3.61 into singlet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 0.77 (−ve, CH_2I), 19.48 (+ve, CH_3), 57.24 (+ve, CH-4), 80.10 (+ve, CH-5), 76.87 (absent, C-3), 127.23 (+ve, CH), 128.16 (+ve, CH), 128.56 (+ve, CH), 135.16 (absent, C), 176.58 (absent, C═O); IR ν_{max} (KBr): 1772 (C═O), 3404 (OH) cm^{-1}. (Found: C, 43.5; H, 4.1. $C_{12}H_{13}IO_3$ requires C, 43.37; H, 3.92%).

4.4.10. (3*S,4*S**,5*R**)-3-Hydroxy-3-phenyl-4-ethoxycarbonyl-5-iodomethyl-furan-2(5*H*)-one (21).** *Procedure C*. 807 mg, 69%; light yellow liquid; FAB mass M^+ *m/z* 390 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.05 (t, $J=7.2$ Hz, 3H, CH_3), 1.67 (br s, 1H, OH, exchanges with D_2O), 3.45 (dd, $J_1=11.4$ Hz, $J_2=4.8$ Hz, 1H, 1H of CH_2I), 3.62 (d, $J=9$ Hz, 1H, CH), 3.66 (dd, $J_1=11.4$ Hz, $J_2=4.8$ Hz, 1H, 1H of CH_2i), 3.88–3.93 (m, 2H, OCH_2), 4.64–4.69 (m,1H, CH), 7.28–7.45 (m, 5*H*, Arh); *Decoupling*: the decoupling of 1H multiplet (δ 4.64–4.69) converts double doublet at δ 3.45 and δ 3.66 into doublet and doublet at δ 3.62 into singlet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 5.83 (−ve, CH_2I), 13.77 (+ve, CH_3), 59.04 (+ve, CH), 61.77 (−ve, CH_2), 75.62 (+ve, CH), 80.16 (ab, C), 125.12 (+ve, CH), 128.79 (+ve, CH), 129.48 (+ve, CH), 136.34 (ab, C), 167.16 (ab, C), 175.02 (ab, C). IR ν_{max} (neat): 1726 (C═O), 1787 (C═O), 3614 (OH) cm^{-1}. (Found: C, 43.2; H, 3.9. $C_{14}H_{15}IO_5$ requires C, 43.10; H, 3.87%).

4.5. X-ray crystal data collection for 19a and 19b

X-ray crystal data was measured by using θ–2θ scan mode. The structures were solved by using direct method SHELX-97.

4.5.1. Compound 19a. CCDC 261510, Mol. formulae $C_{17}H_{15}IO_3$; triclinic space group *P*-1, $a=8.039$ Å, $b=10.102$ Å, $c=10.590$ Å, $\alpha=88.40(13)°$, $\beta=80.13(13)°$, $\gamma=70.17(15)°$, $V=796.6(2)$ Å^3, $z=2$, dc = 1.643 mg/m^3, Mo Kα = 0.70930 Å, θ range for data collection 1.95–24.97°. The structure solution is based on 3021 reflections, which converged to $R=0.037$. Refinement method: full-matrix least squares on *F*2, goodness of fit = 1.105.

4.5.2. Compound 19b. CCDC 261098, Mol. formulae $C_{17}H_{15}IO_3$; triclinic space group *P*-1, $a=8.3040(14)$ Å, $b=9.6450(15)$ Å, $c=10.6990(17)$ Å, $\alpha=76.422(13)°$, $\beta=89.511(13)°$, $\gamma=70.592(15)°$, $v=783.4(2)$ Å^3 , $z=2$, dc = 1.671 mg/m^3, Mo Kα = 0.70930 Å, θ range for data collection 1.96–24.93°. The structure solution is based on 2636 reflections, which converged to $R=0.023$. Refinement method: full-matrix least squares on *F*2, goodness of fit = 1.069.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.06.045

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