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Novel cyclization cascades to functionalized indanes and tetrahydronaphthalenes

Zulfiqar A. Khan [a], Michio Iwaoka [b], Thomas Wirth [a,*]

[a] School of Chemistry, Cardiff University, Park Place, Cardiff CF10 3AT, UK
[b] Department of Chemistry, School of Science, Tokai University, Kitakaname, Hiratsuka-shi, Kanagawa 259-1292, Japan

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ABSTRACT

Cyclization cascades involving C–C bond formations followed by lactonization reactions provide fast access to structurally complex tricyclic indane and tetrahydronaphthalene derivatives.

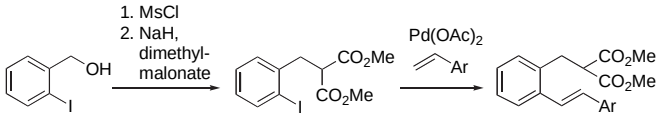
1. Introduction

The formation of new carbon–carbon bonds by carbocyclizations has been an attractive area of research and proven to be a useful tool for the synthesis of carbocyclic molecules.[1] The medicinal importance of molecules possessing indane[2] and 1,2,3,4-tetrahydronaphthalene moieties[3] is well documented. Strigolactones are a group of sesquiterpene lactones and their synthetic analogues can act as hormone stimulants for seed-germination/symbiotic fungi and even as shoot branching inhibitors.[4] Indane derivatives have also been used as versatile ligands in asymmetric ruthenium catalyzed transfer hydrogenation reaction of ketones.[5] There are various methods available for the synthesis of indane and tetrahydronaphthalene skeletons. Common routes for the synthesis of tetrahydronaphthalenes are by hydrogenation of naphthalenes,[6] by Friedel–Crafts alkylations,[7] by dehydration of alcohols,[8] or by gold-catalyzed benzannulations of 3-hydroxy-1,5-enynes.[9] Indane and tetrahydonaphthalene can also be synthesized by reduction of indanones and 3,4-dihydronaphthalen-1(2*H*)ones.[10] Straightforward approaches for the synthesis of indanes are [3+2] cycloadditions of benzyl cations with styrenes[11] or palladium catalyzed intramolecular carboannulation reactions.[12] However, some drawbacks present in these classical methods include the use of expensive transition metal catalysts, the use of strong acidic conditions or sometimes high reaction temperatures. Therefore, facile and effective methods for the synthesis of indanes and tetrahydronaphthalenes are still sought after.

2. Results and discussion

Recently we have reported the synthesis of indene derivatives by iodine mediated *endo*-cyclizations of malonate moieties onto alkynes.[13] In our efforts towards the synthesis of carbocycles we report herein the synthesis of indane and 1,2,3,4-tetrahydronaphthalene derivatives by iodine mediated carboannulations of stilbene derivatives with a subsequent cascade reaction leading to indene and tetrahydronaphthalene-based tricyclic lactone derivatives.

The stilbene derivatives used in this investigation were synthesized from 2-iodobenzyl alcohol **1** by mesylation and addition of dimethylmalonate to give derivative **2**, followed by a Heck reaction to **3** similar to compounds prepared for selenium mediated cyclizations (Scheme 1).[14] Alternatively, a Heck reaction can be performed using ethyl 2-iodobenzoate. After reduction with lithium aluminium hydride a similar sequence of mesylation and reaction with dimethylmalonate can be carried out to provide compounds of type **3**.



Scheme 1. Synthesis of the cyclization precursors **3.**

* Corresponding author. E-mail address: wirth@cf.ac.uk (T. Wirth).

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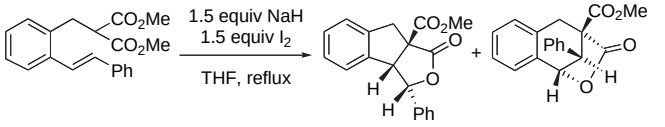
Different reagent combinations were screened to find optimal reaction conditions for the iodine-mediated carbocyclization of **3a**. Compound **3a** (Ar=Ph) was treated with NaH followed by addition of ICl and heated at reflux for one hour, which resulted in the formation of some addition of iodine monochloride to the double bond, but carbocyclic products were not obtained (Table 1, entry 1). Reaction of compound **3a** with iodine and pyridine led to the complete recovery of starting material (Table 1, entry 2). When compound **3a** was treated with bis(trifluoroacetoxyiodo)benzene, an unidentified mixture of products was formed (Table 1, entry 3). Reaction of **3a** with sodium hydride followed by iodine[15] resulted in the formation of two products, **4a** and **5a** in 70% combined yield (Table 1, entry 4).

Table 1
Cyclization of **3a** to indene **4a** and tetrahydronaphthalene **5a**



3a **4a** **5a**

Entry	Reagent	Base	Time [h][a]	Yield of **4a** [%]	Yield of **5a** [%]
1	ICl	NaH	1	0	0
2	I_2	Pyridine	3	0	0
3	$PhI(OCOCF_3)_2$	—	16[b,c]	0	0
4	I_2	NaH	1.5	52	18
5	I_2	KO^tBu	30[b]	48	15
6	I_2	K_2CO_3	4.5	28	34

[a] Reaction performed at 65 °C.
[b] Reaction performed at 20 °C.
[c] The reaction was carried out in dichloromethane instead of THF.

The same two products **4a** and **5a** were observed when exchanging the base to potassium *tert*-butoxide and performing the reaction at room temperature (Table 1, entry 5). *tert*-Butyl hypoiodite[16] is formed upon reaction of iodine with potassium *tert*-butoxide, a versatile reagent for electrophilic[17] but also for radical functionalizations.[18] Using a weaker base such as potassium carbonate (Table 1, entry 6) resulted in an increased amount of cyclization product **5a**.

The products **4a** and **5a**, resulting from either an initial 5-*exo*-*trig* cyclization leading to **4a**, or a 6-*endo*-*trig* cyclization leading to **5a** can be separated by column chromatography. Both compounds are formed as single diastereomers as judged from their NMR spectra. Product **4a** is a colourless crystalline compound and the stereochemistry was confirmed by X-ray analysis as shown in Figure 1.[19]

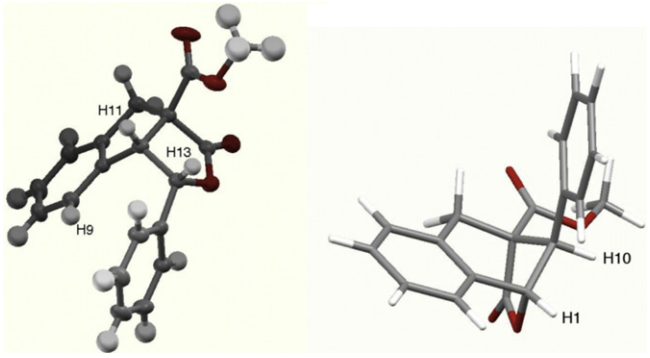
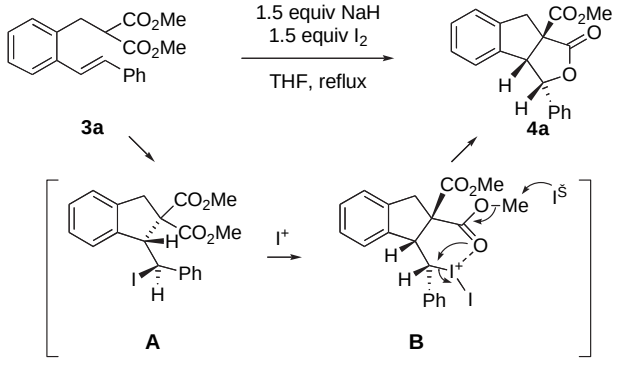


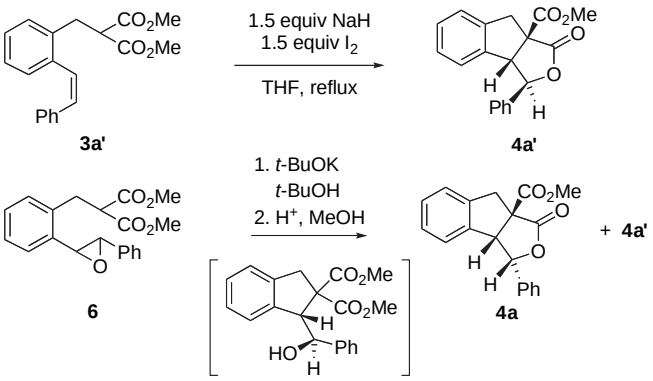
Figure 1. X-ray structure of **4a** and optimized structure **5a** by calculation.

The *cis*-relationship between hydrogens H11 and H13 is remarkable. Therefore, the reaction sequence cannot consist of an iodocarbocyclization followed by an S_N2 substitution of the iodine with one of the ester moieties, as this would lead to a *trans*-arrangement of these two hydrogen atoms. Such sequences have already been reported.[20] A subsequent S_N1 type substitution is very unlikely under the reaction conditions and should lead to the thermodynamically favoured *trans*-isomer (the *cis*-isomer **4a** is about 0.22 kcal/mol higher in energy).[21] Under the reaction conditions we suggest an activation of the iodine in **A** by reaction with an iodonium cation followed by a reductive elimination of **B** towards the tricyclic lactone derivative **4a** as shown in Scheme 2. This is regarded as a ligand coupling of the substituents on the iodine with retention of configuration, which can also be observed with other hypervalent compounds[22] and with metal catalysts.[23] The close proximity to the phenyl substituent as evidenced by the X-ray structure (Fig. 1) leads to a high-field shift of proton H9, which is observed at δ=5.57 ppm. Alternatively, the observed *cis*-isomer **4a** could be explained by an initial diiodination of alkene **3a** followed by two subsequent S_N2 reactions.



Scheme 2. Suggested mechanism for the formation of **4a**.

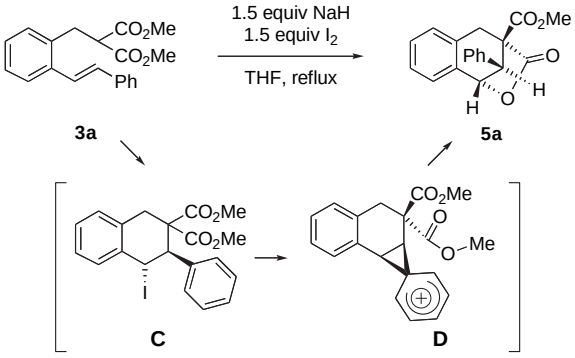
The reaction of the (*Z*)-stilbene derivative **3a′** under identical reaction conditions led to the tricyclic lactone **4a′** as shown in Scheme 3. The reaction of **3** to **4** is a stereospecific reaction and in additional experiments it was confirmed that no epimerization is taking place under the reaction conditions. Related compounds to **4** have been synthesized recently using lithiated aryloxiranes and alkylidene malonates.[24] Compound **3a** was epoxidized with *m*CPBA in 95% yield and the resulting epoxide **6** treated with potassium *tert*-butoxide in *tert*-butanol. After re-esterification using methanol and sulfuric acid the compounds **4a** and **4a′** were obtained in 46% overall yield as shown in Scheme 3. Under the reaction conditions, however, epimerization occurred towards the thermodynamically more stable isomer **4a′** and a mixture of **4a** and **4a′** (ratio 1:2) was isolated.



Scheme 3. Mechanistic investigations towards cyclization products **4a** and **4a′**.

NOE experiments of compound **5a** suggest an axial position of the phenyl substituent, as irradiation at H10 resulted only in an NOE at H1. Furthermore, the calculated structure **5a** (Fig. 1) indicated a dihedral angle H1–C–C–H10 of 50°, whereas calculations

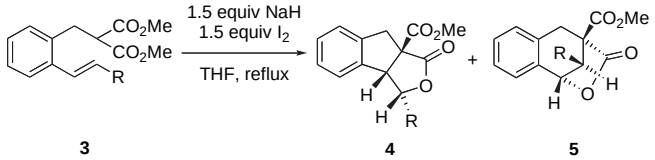
of the stereoisomer with an equatorial phenyl substituent showed a dihedral angle of 88°. The coupling constant between H1 and H10 was determined to be J=3.0 Hz, which, according to the Karplus equation, matches with a torsion angle of 50°. In addition, ab-initio calculations of the NMR shifts of the two different stereoisomers showed best correlation with isomer **5a** providing further proof of the structure. The *cis*-arrangement of the hydrogens H1 and H10 is noteworthy, as such an isomer cannot be formed by a simple S_N2 displacement of the iodine in **C** after the initial iodocyclization reaction. In order to account for the observed stereochemistry, we suggest the activation of the iodine in **C** by another iodine electrophile and a participation of the phenyl substituent. This will lead to the intermediate phenonium ion **D**, which is then opened to **5a** as shown in Scheme 4. The involvement of phenonium ions in iodine mediated cyclizations has already been reported.[25]



Scheme 4. Suggested mechanism for the formation of **5a**.

In order to further evaluate the scope of this reaction a range of different substituted compounds **3** were prepared according to Scheme 1 and subjected to similar reaction conditions. The products **4** and **5** are formed in this reaction with consistent good overall yields (47–79%). Depending on the substituent, different ratios of **4**:**5** have been observed as shown in Table 2.

Table 2
Cyclization of stilbenes **3** to indanes **4** and tetrahydronaphthalenes **5**



Entry	R	Time [h]	Yield of **4** [%]	Yield of **5** [%]	Ratio **4**:**5**
1	**3a**: Ph	1.5	52	18	3:1
2	**3b**: 4-Me–C_6H_4	3	53	24	2:1
3	**3c**: 1-Naphthyl	3.5	18	55	1:3[a]
4	**3d**: 2-Naphthyl	3	55	19	3:1
5	**3e**: 2-Cl–C_6H_4	3	20	59	1:3[a]
6	**3f**: 4-Cl–C_6H_4	3	37	37	1:1[a]
7	**3g**: 2,6-Cl_2–C_6H_3	2.5	47	0	1:0

[a] The product mixture of **4** and **5** could not be separated, ratio determined by ^{1}H NMR spectroscopy.

The ratio of *exo* cyclization (leading to **4**) and *endo*-cyclization (leading to **5**) is influenced by the nature of the substituent R. The preference of an *exo*-cyclization over an *endo*-cyclization is found for most substrates. The *ortho*-disubstituted derivative **3g** leading exclusively to the *exo*-cyclized product **4g** (Table 2, entry 7) could be seen as another proof for the mechanism depicted in Scheme 3. The formation of a phenonium intermediate is not possible with **3g**. Compounds **3** with one substituent in the *ortho*-position were found to react preferentially via an *endo*-cyclization route as evidenced by **3c** (R=1-naphthyl, Table 2, entry 3) and **3e** (R=2-Cl–C_6H_4, Table 2, entry 5) with a ratio of about 1:3 for the *exo*/*endo* cyclization.

In conclusion, we have developed cyclization cascades of stilbene derivatives with iodine electrophiles, which afforded novel indane and tetrahydonaphthalene compounds in a one-pot reaction from simple starting materials. We report an intramolecular carbon–carbon bond formation promoted by iodine electrophiles via either 5-*exo*- or 6-*endo*-*trig* cyclizations and a detailed investigation of the subsequent lactonization with a unique stereochemical outcome. The synthetic potential of the novel structures is presently being explored.

3. Experimental section

3.1. 1-Vinylnaphthalene[26]

A mixture of CH_3PPh_3Br (12.9 mmol, 4.61 g) and KO^{t}Bu (14 mmol, 1.57 g) in dry toluene (30 mL) was stirred at 0 °C for 30 min and at rt for 4 h. The reaction mixture was cooled to 0 °C followed by addition of 1-naphthaldehyde (11.8 mmol, 1.84 g). The reaction mixture was stirred overnight at rt. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using hexane as eluent to yield (11.8 mmol, 1.81 g, quantitative) 1-vinylnaphthalene as colourless oil. The spectroscopic data are in agreement with literature.[26]

3.2. General procedure for Heck reactions (GP1)[27]

A mixture of methyl 2-iodobenzoate (15 mmol, 4.0 g), styrene (18.0 mmol, 1.87 g), triethylamine (32.0 mmol, 4.4 mL), palladium acetate (0.48 mmol, 323 mg) and triphenylphosphine (0.96 mmol, 251 mg) were heated under reflux at 110 °C for 5 h. Solid products were isolated by diluting the reaction mixtures with 200 ml of 10% aq hydrochloric acid with stirring to dissolve the salts and excess amine. The crude product was extracted with ethyl acetate (3×20 mL). The combined organic phases were dried with $MgSO_4$ and evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (EtOAc/hexane 1:12).

3.3. (*E*)-Methyl 2-styrylbenzoate[28]

The title compound was obtained according to **GP1** and isolated as yellow oil in 87% yield (13.2 mmol, 3.15 g) after purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.03 (1H, d, J=16.0 Hz, CH=*CH*–Ph), 7.97 (1H, d, J=8.0 Hz, Ar–*H*), 7.76 (1H, d, J=8.0 Hz), 7.60 (2H, d, J=7.5 Hz), 7.54 (1H, t, J=8.0 Hz), 7.31–7.42 (4H, m), 7.04 (1H, d, J=16.0 Hz, *CH*=CH–Ph), 3.96 (3H, s, COO*CH*$_3$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=167.9, 139.3, 137.5, 132.2, 131.5, 130.7, 128.7 (2×C), 128.6, 127.9, 127.5, 127.2, 127.0, 126.9 (2×C), 52.2 ppm. The spectroscopic data are in agreement with literature.[28]

3.4. (*E*)-Methyl 2-(4-methylstyryl)benzoate[14]

The title compound was obtained according to **GP1** as colourless crystals in 80% yield (12 mmol, 3.02 g) after purification.

Mp: 74 °C; (lit. mp: 74 °C);[14] ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.87 (1H, d, J=16.2 Hz), 7.84 (1H, d, J=8.0 Hz), 7.64 (1H, d, J=8.0 Hz), 7.44 (1H, t, J=7.5 Hz), 7.37 (2H, d, J=8.0 Hz), 7.23 (1H, t, J=7.5 Hz), 7.10 (2H, d, J=7.5 Hz), 6.92 (1H, d, J=16.2 Hz, CH=*CH*), 3.85 (3H, s, COO*CH*$_3$), 2.29 (3H, s, Ar*CH*$_3$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=168.0, 139.4, 137.8, 134.7, 132.1, 131.4, 130.7, 129.4 (2×C), 128.5, 127.0, 126.9, 126.8 (2×C), 126.4, 52.1, 21.3 ppm; IR (ν):=3041, 2936, 1761, 1715, 1591, 1510, 1289, 1255, 1242, 1126, 1073, 962, 804, 740 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{17}O_2$: 253.1223; found: 253.1222.

3.5. General procedure for the reduction of 2-substituted stilbenes (GP2)[1b,29,30]

A solution of the corresponding ester (9 mmol) in dry diethyl ether (20 mL) was added to suspension of $LiAlH_4$ (10.8 mmol, 410 mg) in dry diethyl ether (100 mL) at 0 °C. After stirring for 2 h, the reaction was quenched with aq Na_2SO_4 solution (20 mL). After drying the organic phase with $MgSO_4$ the residue was purified by flash chromatography with petroleum ether/ethyl acetate (4:1) as eluent to give corresponding alcohols in good yields.

3.6. (*E*)-(2-Styrylphenyl)methanol[14]

The title compound was obtained according to **GP2** by the reaction of corresponding ester (9 mmol, 2.2 g) with $LiAlH_4$ (10.8 mmol, 0.41 g) to give 92% yield (8 mmol, 1.74 g) of the alcohol as colourless crystals after purification.

Mp: 103 °C; (lit. mp: 103 °C);[14] ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.69 (1H, d, *J*=7.5 Hz), 7.56 (2H, d, *J*=7.5 Hz), 7.48 (1H, d, *J*=16.2 Hz, C*H*=CH–Ph), 7.42–7.30 (6H, m), 7.04 (1H, d, *J*=16.2 Hz, CH=C*H*–Ph), 4.86 (2H, s, CH_2OH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=137.9, 137.4, 136.4, 131.3, 128.7 (2×C), 128.6, 128.3, 127.9, 127.8, 126.7 (2×C), 126.0, 125.4, 63.7 ppm. Spectroscopic data are in agreement with literature.[31]

3.7. (*E*)-(2-(4-Methylstyryl)phenyl)methanol[14]

The title compound was obtained according to **GP2** by the reaction of corresponding ester (9 mmol, 2.2 g) with $LiAlH_4$ (10.8 mmol, 0.41 g) gave 88% yield (7.9 mmol, 1.78 g) as colourless crystals after purification.

Mp: 127 °C; (lit. mp: 127 °C);[14] ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.57 (1H, d, *J*=7.2 Hz), 7.35 (2H, d, *J*=8.0 Hz), 7.30–7.19 (4H, m), 7.11–7.09 (2H, m), 6.95 (1H, d, *J*=16.0 Hz), 4.75 (2H, s, CH_2OH), 2.29 (3H, s, ArCH_3) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=137.80, 137.75, 136.6, 134.6, 131.2 (2×C), 129.4, 128.6, 128.3, 127.6, 126.6 (2×C), 125.9, 124.3, 63.7, 21.3 ppm; IR (ν):=3356, 3276, 3025, 2917, 2863, 1512, 1478, 1044 cm^{-1}; HRMS calcd for $C_{16}H_{20}ON$: 242.1539; found: 242.1540.

3.8. General procedure for the synthesis of malonate derivatives (GP3)

To a solution of the corresponding alcohol (7.0 mmol) in CH_2Cl_2 (25 mL) were added Et_3N (9.0 mmol, 0.9 g) and methanesulfonyl chloride (8.0 mmol, 0.91 g) at 0 °C. After being stirred for 1 h at rt the mixture was poured into 10% aq HCl (15 mL) and extracted with ether (3×15 mL). The combined organic phases were dried on $MgSO_4$ and evaporated under reduced pressure. The mesylate was dissolved in dry THF (5 mL) and added to a solution of NaH (60% in mineral oil, 9.0 mmol, 0.36 g) and dimethylmalonate (9 mmol, 1.18 g) in THF (30 mL), then the reaction mixture was heated at reflux for 6–36 h. The mixture was poured into 10% aq HCl (15 mL) and extracted with ether (3×20 mL). The combined ether extracts were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was subjected to flash chromatography (12:1 hexane/EtOAc) to give the malonate derivatives.

3.9. Dimethyl 2-(2-iodobenzyl)malonate (2)[32]

The title was prepared according to **GP3** by the reaction of 2-iodobenzyl alcohol 1 (11 mmol, 2.85 g) in 68% yield (8.28 mmol, 2.88 g) as colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ=7.84 (1H, d, *J*=8.0 Hz), 7.28–7.24 (2H, m), 6.93 (1H, t, *J*=8.0 Hz), 3.88 (1H, t, *J*=7.8 Hz), 3.72 (6H, s, COOCH_3), 3.35 (2H, d, *J*=7.8 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=168.9 (2×C), 140.2, 139.8, 130.5, 128.8, 128.4, 100.4, 52.6, 51.6, 39.4 (2×C) ppm; IR (ν): 2951, 1735, 1467, 1434, 752 cm^{-1}; Spectroscopic data are in agreement with literature.[32]

3.10. (*E*)-Dimethyl 2-(2-styrylbenzyl)malonate (3a)

The title compound was prepared by **GP3** starting from corresponding alcohol (9.52 mmol, 2 g) as yellow oil in 40% yield (3.79 mmol, 1.23 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ=7.64 (1H, d, *J*=8.0 Hz), 7.57 (2H, d, *J*=8.0 Hz), 743–7.39 (3H, m), 7.32–7.29 (2H, m), 7.22 (2H, d, *J*=7.5 Hz) 7.04 (1H, d, *J*=16.0 Hz), 3.73–3.70 (m, 7H, CH_2CH- and 2×COOCH_3), 3.43 (2H, d, CH_2CH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.3 (2×C), 137.4, 136.4, 135.5, 131.2, 130.2, 128.8 (2×C), 127.9, 127.8, 127.5, 126.7 (2×C), 126.1, 125.4, 52.9, 52.7, 32.4 (2×C) ppm; IR (ν): 3022, 2944, 2840, 1739, 1595, 1491, 1436, 1341, 1280, 1228, 1155, 1025, 965, 762, 693 cm^{-1}; HRMS (ES): $[M+NH_4]^+$ calcd for $C_{20}H_{24}NO_4$: 342.1700; found: 342.1702.

3.11. (*E*)-Dimethyl 2-(2-(4-methylstyryl)benzyl)malonate (3b)

The title compound was prepared by **GP3** starting from corresponding alcohol (7.5 mmol, 1.68 g) as yellow oil in 53% yield (3.96 mmol, 1.34 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ=7.52 (1H, d, *J*=7.5 Hz), 7.36 (2H, d, *J*=8.0 Hz), 7.26 (1H, d, *J*=16.0 Hz), 7.17–7.15 (2H, m), 7.11 (3H, d, *J*=7.5 Hz), 6.92 (1H, d, *J*=16 Hz), 3.62–3.60 (m, 7H, CH_2CH– and 2×COOCH_3), 3.32 (2H, d, *J*=7.5 Hz), 2.29 (3H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.3 (2×C), 137.8, 136.5, 135.4, 134.7, 131.1, 130.2, 129.5 (2×C), 127.6 (2×C), 127.4, 126.6, 126.0, 124.4, 52.9, 52.6, 32.4 (2×C), 21.3 ppm; IR (ν): 3024, 2953, 1750, 1736, 1511, 1435, 1023 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{26}NO_4$: 356.1856; found: 356.1855.

3.12. (*E*)-Dimethyl 2-(2-(2-(naphthalen-1-yl)-vinyl)benzyl)malonate (3c)

The title compound was prepared by Heck reaction of compound **2** (1.43 mmol, 0.5 g) with 1-vinylnaphthalene (1.71 mmol, 0.26 g) according to **GP1** as yellow oil in 89% yield (1.25 mmol, 0.47 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ=8.14 (1H, d, *J*=8.0 Hz), 7.80 (1H, d, *J*=7.5 Hz), 7.75–7.70 (3H, m), 7.65 (1H, d, *J*=7.5 Hz), 7.48–7.42 (3H, m), 7.33 (1H, d, *J*=16.0 Hz), 7.25–7.15 (3H, m), 3.65 (1H, t, *J*=7.5 Hz, CH_2CH), 3.58 (6H, s, 2×COOCH_3), 3.35 (2H, d, *J*=7.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.2 (2×C), 136.8, 135.6, 135.0, 133.8, 131.4, 130.2, 128.7, 128.6, 128.4, 128.3, 127.9, 127.5, 126.5, 126.2, 125.9, 125.8, 123.9, 123.8, 52.9, 52.6, 32.3 (2×C) ppm; IR (ν): 3032, 2925, 2851, 1750, 1736, 1437, 1221 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{24}H_{26}NO_4$: 392.1856; found: 392.1858.

3.13. (*E*)-Dimethyl 2-(2-(2-(naphthalen-2-yl)-vinyl)benzyl)malonate (3d)

The title compound was prepared by Heck reaction of compound **2** (1.43 mmol, 0.5 g) with 2-vinylnaphthalene (1.71 mmol, 0.26 g) according to **GP1** as colourless crystalline solid in 76% yield (1.09 mmol, 0.41 g).

Mp: 133–134 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.91–7.81 (5H, m), 7.71 (1H, d, *J*=8.0 Hz), 7.57 (1H, d, *J*=16 Hz), 7.50 (2H, t, *J*=7.5 *Hz*), 7.34–7.26 (3H, m), 7.24 (1H, d, *J*=16 *Hz*), 3.77 (1H, t, *J*=8.0 Hz, CH_2CH), 3.73 (6H, s, 2×COOCH_3), 3.49 (2H, d, *J*=7.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.3 (2×C), 136.4, 135.6, 134.9, 133.7, 133.2, 131.3, 130.3, 128.4, 128.1, 127.82, 127.75, 127.5, 126.9, 126.4, 126.09, 126.05, 125.8, 123.6, 53.0, 52.6, 32.4 (2×C) ppm; IR (ν): 3031,

2924, 2851, 1751, 1733, 1436, 1220 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{24}H_{26}NO_4$: 392.1856; found: 392.1858.

3.14. (*E*)-Dimethyl 2-(2-(2-chlorostyryl)benzyl)malonate (3e)

The title compound was prepared by a Heck reaction of compound **2** (1.43 mmol, 0.5 g) with 2-chlorostyrene (1.71 mmol, 237 mg) according to **GP1** as yellow oil in 73% yield (1.06 mmol, 0.38 g).

^1H NMR (500 MHz, $CDCl_3$): δ=7.77 (1H, d, J=8.0 Hz), 7.69 (1H, d, J=7.5 Hz), 7.44–7.40 (3H, m), 7.32–7.28 (3H, m), 7.26–7.22 (2H, m), 3.73–3.71 (7H, m, CH_2CH- and 2×$COOCH_3$), 3.44 (2H, d, J=7.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.2 (2×C), 136.2, 135.7, 135.5, 133.5, 130.2, 129.9, 128.7, 128.2, 128.1, 127.5, 127.2, 127.0, 126.8, 126.5, 53.0, 52.6, 32.2 (2×C) ppm; IR (ν): 3063, 3015, 2954, 2928, 2870, 1740, 1723, 1483, 1251, 1161 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{23}ClNO_4$: 376.1310; found: 376.1315.

3.15. (*E*)-Dimethyl 2-(2-(4-chlorostyryl)benzyl)malonate (3f)

The title compound was prepared by a Heck reaction of compound **2** (1.43 mmol, 0.5 g) with 4-chlorostyrene (1.71 mmol, 237 mg) according to **GP1** as yellow oil in 72% yield (1.04 mmol, 358 mg).

^1H NMR ($CDCl_3$, 500 MHz): δ=7.52 (1H, d, J=7.5 Hz), 7.39 (2H, d, J=8.5 Hz), 7.31–7.26 (3H, m), 7.14–7.11 (3H, m), 6.89 (1H, d, J=16 Hz), 3.62–3.60 (7H, m, CH_2CH– and 2×$COOCH_3$), 3.32 (2H, d, J=7.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.2 (2×C), 136.0, 135.9, 135.6, 133.4, 130.2, 129.8, 128.9 (2×C), 128.0, 127.9 (2×C), 126.1 (2×C), 52.9, 52.7, 32.3 (2×C) ppm; IR (ν): 3028, 2952, 2844, 1749, 1736, 1599, 1435, 1229 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{23}ClNO_4$: 376. 1310; found: 376.1314.

3.16. (*E*)-Dimethyl 2-(2-(2,6-dichlorostyryl)benzyl)-malonate (3g)

The title compound was prepared by Heck reaction of compound **2** (1.43 mmol, 0.5 g) with 2,6-dichlorostyrene (1.71 mmol, 296 mg) according to **GP1** as yellow oil in 66% (0.37 g) as a yellow crystalline solid.

Mp: 82–83 °C; ^1H NMR (500 MHz, $CDCl_3$): δ=7.69 (1H, d, J=8.0 Hz), 7.35 (1H, d, J=16.5 Hz), 7.29 (2H, d, J=8.0 Hz, Ar–H), 7.24–7.12 (3H, m), 7.05 (1H, dd, J=8.0 Hz), 6.95 (1H, d, J=16.5 Hz), 3.69 (1H, t, J=6.5 Hz), 3.61 (6H, s, $COOCH_3$), 3.29 (2H, d, J=6.5 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.2 (2×C), 136.2, 135.7, 134.61, 134.57, 134.1, 130.3, 128.6 (2×C), 128.33, 128.25, 127.5, 126.6, 125.3, 52.8, 52.6, 32.3 (2×C) ppm; IR (ν): 3063, 3015, 2954, 2928, 2841, 1740, 1723, 1578, 1483, 1251, 1222 cm^{-1}; HRMS: calcd for $C_{20}H_{22}O_4Cl_2N$: 410.0920; found: 410.0926.

3.17. General procedure for the double cyclization to indanes and tetrahydronaphthalenes (GP4)

Sodium hydride (0.285–0.475 mmol [1.5–2.5 equiv]) was added to a solution of stilbene malonate (0.19 mmol) in THF (15 mL) and the reaction mixture was stirred for five minutes at rt. Iodine (0.285–0.475 mmol [1.5–2.5 equiv]) was added to the reaction mixture, which was then heated at reflux for 1.5–3.5 h. The reaction mixture was cooled to rt and a saturated solution of $Na_2S_2O_3$ (10 mL) was added. The aqueous layer was extracted with ether (2×15 mL). The combined organic phases were washed with water (2×5 mL) and brine (4 mL). After evaporation of the solvent in vacuum the crude mixture was purified by flash chromatography (EtOAc/hexane 1:20). For some experiments KO^tBu (0.285 mmol (1.5 equiv)) and K_2CO_3 (0.57 mmol (3 equiv)) were used as bases instead of NaH (Table 1, entries 5 and 6).

3.18. *rac*-(3*S*,3a*R*,8a*S*)-Methyl 1-oxo-3-phenyl-3,3a,8,8a-tetrahydro-1*H*-indeno[2,1-*c*]furan-8a-carboxylate (4a)

The title compound was prepared by using compound **3a** (0.19 mmol, 62 mg) as starting material according to **GP4** as colourless crystalline solid in 52% yield (0.097 mmol, 30 mg).

Mp: 131 °C; ^1H NMR ($CDCl_3$, 500 MHz): δ=7.30–7.28 (3H, m), 7.12 (3H, d, J=7.5 Hz), 7.07 (1H, t, J=7.5 Hz), 6.72 (1H, t, J=7.5 Hz), 6.08 (1H, d, J=6.3 Hz), 5.57 (1H, d, J=8.0 Hz), 4.41 (1H, d, J=6.3 Hz), 3.85 (3H, s, $COOCH_3$), 3.64–3.62 (2H, m, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.4, 169.3, 141.0, 135.7, 134.9, 128.7, 128.43, 128.40 (2×C), 126.8, 126.4, 126.2 (2×C), 124.6, 83.0, 62.5, 56.9, 53.5, 39.2 ppm; IR (ν): 3066, 2917, 2947, 1775, 1734, 1481, 1436, 1247, 1150 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{20}NO_4$: 326.1387; found: 326.1390.

3.19. (1*S*,4*S*,10*S*)-Methyl 3-oxo-10-phenyl-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5a)

The title compound was prepared by using compound **3a** (0.19 mmol, 62 mg) as starting material according to **GP4** as yellow oil in 18% yield (0.033 mmol, 11 mg).

^1H NMR ($CDCl_3$, 500 MHz): δ=7.39–7.37 (3H, m), 7.32–7.20 (6H, m), 5.49 (1H, d, J=3 Hz), 4.31 (1H, d, J=3.0 Hz), 3.80–3.45 (2H, m), 3.55 (3H, s, $COOCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.3, 170.0, 140.7, 139.9, 139.0, 128.9, 128.8 (2×C), 128.5, 128.1, 125.2 (2×C), 125.1, 123.9, 86.0, 60.5, 60.0, 53.2, 40.5 ppm; IR (ν): 2954, 2923, 1784, 1736, 1625, 1541, 1247, 1035 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{20}NO_4$: 326.1387; found: 326.1390.

NOE Experiment on compound **5a**: The proton at 4.31 ppm (H^1) was irradiated and only a 4.93% enhancement in the signal for proton at 5.49 ppm (H^{10}) was observed.

3.20. (3*S*,3a*R*,8a*S*)-Methyl 1-oxo-3-(*p*-tolyl)-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4b)

The title compound was prepared by using compound **3b** (0.19 mmol, 64 mg) as starting material according to **GP4** as colourless crystalline solid in 53% yield (0.1 mmol, 32 mg).

Mp: 136 °C; ^1H NMR ($CDCl_3$, 500 MHz): δ=7.13–7.08 (4H, m), 6.99 (2H, d, J=7.5 Hz), 6.74 (1H, t, J=7.5 Hz), 6.05 (1H, d, J=6.5 Hz), 5.64 (1H, J=7.5 Hz), 4.38 (1H, d, J=6.5 Hz), 3.84 (3H, s, $COOCH_3$), 3.58–3.63 (2H, m), 2.32 (3H, s, $ArCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.4, 169.4, 141.0, 138.5, 135.8, 131.8, 129.1 (2×C), 128.3, 126.9, 126.4, 126.2 (2×C), 124.5, 83.1, 62.5, 56.9, 53.5, 39.2, 21.3 ppm; IR (ν): 3025, 2956, 2925, 2853, 1770, 1735, 1431, 1252 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{22}NO_4$: 340.1543; found: 340.1539.

3.21. (1*S*,4*S*,10*S*)-Methyl 3-oxo-10-(*p*-tolyl)-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5b)

The title compound was prepared by using compound **3b** (0.19 mmol, 64 mg) as starting material according to **GP4** as yellow oil in 24% yield (0.043 mmol, 14.0 mg).

^1H NMR ($CDCl_3$, 500 MHz): δ=7.27–7.24 (5H, m), 7.17–7.08 (3H, m), 5.44 (1H, d, J=3.0 Hz), 4.29 (1H, d, J=3.0 Hz), 3.85 (3H, s, $COOCH_3$), 3.83–3.60 (2H, m), 2.31 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.3, 170.1, 140.8, 139.9, 138.3, 136.0, 129.5 (2×C), 128.8, 128.1, 125.2 (2×C), 125.1, 123.9, 86.2, 60.7, 60.0, 53.2, 40.5, 21.2 ppm; IR (ν): 2952, 2924, 1780, 1739, 1608, 1516, 1435, 1246 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{22}NO_4$: 340.1543; found: 340.1539.

3.22. (3*R*,3a*S*,8a*R*)-Methyl 3-(naphthalen-1-yl)-1-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4c) and (1*S*,4*S*,10*S*)-Methyl 10-(naphthalen-1-yl)-3-oxo-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5c)

The title compounds were prepared by using compound **3c** (0.19 mmol, 71 mg) as starting material according to **GP4** as an oil in 72% yield (0.134 mmol, 49 mg) as an inseparable mixture. Ratio of **4c**:**5c** is 18:55 (NMR).

IR (ν): 3055, 2953, 2927, 2853, 1790, 1729, 1601, 1512, 1435, 1246 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{22}NO_4$: 376.1543; found: 376.1545.

3.23. (3*R*,3a*S*,8a*R*)-Methyl 3-(naphthalen-2-yl)-1-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4d)

The title compound was prepared by using compound **3d** (0.19 mmol, 71 mg) as starting material according to **GP4** as colourless crystalline solid in 55% yield (0.10 mmol, 37 mg).

Mp: 183 °C; ^1H NMR ($CDCl_3$, 500 MHz): δ=7.82–7.70 (4H, m), 7.66 (1H, s), 7.48–7.42 (2H, m), 7.18 (1H, d, J=8.0 Hz) 7.13 (1H, d, J=7.5 Hz), 7.04 (1H, t, J=7.5 Hz), 6.25 (1H, d, J=6.5 Hz), 5.54 (1H, d, J=8.0 Hz), 4.50 (1H, d, J=6.5 Hz), 3.87 (3H, s, $COOCH_3$), 3.70–3.65 (2H, m, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.4, 169.3, 141.0, 135.6, 133.3, 133.0, 132.3, 128.4, 128.18, 128.16, 127.9, 126.8, 126.6, 126.56, 126.50, 125.5, 124.6, 123.9, 83.2, 62.6, 56.8, 53.6, 39.2 ppm; IR (ν): 3068, 2917, 2947, 1777, 1732, 1479 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{22}NO_4$: 376.1543; found: 376.1546.

3.24. (1*S*,4*S*,10*S*)-Methyl 10-(naphthalen-2-yl)-3-oxo-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5d)

The title compound was prepared by using compound **3d** (0.19 mmol, 71 mg) as starting material according to **GP4** as yellow oil in 19% yield (0.036 mmol, 13 mg).

^1H NMR ($CDCl_3$, 500 MHz): δ=7.88 (1H, d, J=8.0 Hz), 7.83–7.80 (3H, m), 7.50–7.45 (3H, m), 7.34–7.23 (1H, m), 7.34–7.23 (3H, m), 5.66 (1H, d, J=3.0 Hz), 4.39 (1H, d, J=3.0 Hz), 3.78–3.47 (2H, m), 3.49 (3H, s, $COOCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.4, 170.0, 140.7, 140.0, 136.2, 133.14, 133.10, 129.0, 128.9, 128.14, 128.10, 127.8, 126.8, 126.6, 125.1, 124.3, 123.9, 122.8, 86.1, 60.6, 60.0, 53.2, 40.5 ppm; IR (ν): 3056, 2952, 2932, 2856, 1780, 1736, 1603, 1434, 1245 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{22}NO_4$: 376.1543; found: 376.1546.

3.25. (3*S*,3a*R*,8a*S*)-Methyl 3-(2-chlorophenyl)-1-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4e) and (1*S*,4*S*,10*R*)-Methyl 10-(2-chlorophenyl)-3-oxo-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5e)

The title compounds were prepared by using compound **3e** (0.19 mmol, 68 mg) as starting material according to **GP4** as oil in 79% yield (0.147 mmol, 51 mg) as an inseparable mixture. Ratio of **4e**:**5e** is 20:59 (NMR).

IR (ν): 3062, 2952, 2847, 1785, 1733, 1435, 1244, 1099 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{19}ClNO_4$: 360.0997; found: 360.1002.

3.26. (3*S*,3a*R*,8a*S*)-Methyl 3-(4-chlorophenyl)-1-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4f) and (1*S*,4*S*,10*S*)-Methyl 10-(4-chlorophenyl)-3-oxo-1,3,4,5-tetrahydro-1,4-methanobenzo[*c*]oxepine-4-carboxylate (5f)

The title compounds were prepared by using compound **3f** (0.19 mmol, 68 mg) as starting material according to **GP4** as oil in 74% yield (0.134 mmol, 48 mg) as an inseparable mixture. Ratio of **4f**:**5f** is 1:1 (NMR). IR (ν): 3063, 3028, 2951, 2853, 1778, 1736, 1598, 1493, 1458, 1434, 1411, 1247, 1148 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{19}ClNO_4$: 360.0997; found: 360.1003.

3.27. (3*S*,3a*R*,8a*S*)-Methyl 3-(2,6-dichlorophenyl)-1-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]furan-8a-carboxylate (4g)

The title compound was prepared by using compound **3g** (0.19 mmol, 75 mg) as starting material according to **GP4** as colourless crystalline solid in 47% yield (0.087 mmol, 33 mg).

Mp: 151 °C; ^1H NMR ($CDCl_3$, 500 MHz): δ=7.35 (1H, d, J=8.0 Hz), 7.15–7.11 (3H, m), 7.00 (1H, d, J=8.0 Hz), 6.78 (1H, t, J=8.0 Hz), 6.65 (1H, d, J=8.0 Hz), 5.95 (1H, d, J=7.5 Hz), 4.66 (1H, d, J=8.0 Hz), 3.85 (3H, s, $COOCH_3$), 3.83–3.67 (2H, m) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.1, 169.6, 141.4, 136.9, 136.3, 134.5, 133.8, 130.5, 130.1, 128.4, 128.1, 126.7, 124.9, 124.5, 80.9, 61.2, 54.6, 53.7, 39.4 ppm; IR (ν): 3029, 2952, 2928, 1775, 1747, 1560, 1436, 1284 cm^{-1}; HRMS calcd for $C_{19}H_{14}Cl_2O_4$: 376.0264; found: 376.0265.

3.28. (*E*)- and (*Z*)-1-Bromo-2-(2-phenylethenyl)benzene

To a stirred solution of benzyltriphenylphosphonium chloride (10 mmol, 3.9 g) in dry THF (40 mL) at 0 °C *n*-BuLi (2.5 M solution in hexane, 10 mmol, 4 mL) was added dropwise. The red solution was stirred for 0.5 h. A solution of 2-bromobenzaldehyde (10 mmol, 1.9 g) in dry THF (5 mL) was added dropwise. The reaction solution was warmed to room temperature and stirred for 1 h. After addition of water (100 mL), the reaction mixture was extracted with ethyl acetate (3×30 mL). The organic phases were dried with $MgSO_4$, evaporated under reduced pressure and purified by flash chromatography using petroleum ether as eluent to give the product in 93% yield (9.57 mmol, 2.48 g) as colourless oil containing a mixture of (*E*)- and (*Z*)-isomer (1:2.1).

(*Z*)-1-*Bromo*-2-(2-*phenylethenyl*)*benzene*: ^1H NMR ($CDCl_3$, 500 MHz): δ=6.73 (1H, d, J=12.1 Hz), 6.66 (1H, d, J=12.1 Hz), Rest of signals merged in aromatic region with *E* substrate; IR (ν): 3152, 3057, 2969, 2920, 1597, 1558, 1322 cm^{-1}. The spectroscopic data are in agreement with literature.[33]

3.29. (*E*) and (*Z*)-1-Formyl-2-(2-phenylethenyl)benzene

The Grignard reagent was prepared by refluxing 1-bromo-2-(2-phenylethenyl) benzene (3.86 mmol, 1 g) and magnesium turnings (4.16 mmol, 0.1 g) in dry THF (20 mL) for 2 h. A solution of DMF (0.5 mL) in THF (5 mL) was added slowly. The reaction mixture was allowed to cooled to room temperature. The reaction mixture was further stirred for 3 h. The reaction mixture was quenched with aq NH_4Cl (15 mL) and extracted with diethyl ether (2×20 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and then evaporated under reduced pressure. The crude product was purified by flash chromatography (ethyl acetate/hexane 1:10) and obtained in 68% yield (2.59 mmol, 0.54 g) as a yellow oil containing (*E*) and (*Z*)-isomers in a ratio of 1: 2.1.

(*Z*)-*Isomer*: ^1H NMR (500 MHz, $CDCl_3$): 10.14 (1H, s, C*H*O) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): 192.1 (C=O) ppm; *E*-isomer: ^1H NMR (500 MHz, $CDCl_3$): δ=10.20 (1H, s, C*H*O) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=192.7 (C=O) ppm; Other signals of (*E*)- and (*Z*)-isomers signals are merged. IR (ν): 3081, 3060, 3024, 2957, 2930, 2857, 2745, 1695, 1596, 1566, 1494, 1446, 1193, 697 cm^{-1}. The spectroscopic data are in agreement with literature.[34]

3.30. (*E*) and (*Z*)-2-(Styrylphenyl)methanol

Sodium borohydride (4.71 mmol, 0.17 g) was added to a solution of (*E*)- and (*Z*)-1-formyl-2-(2-phenylethenyl)-benzene (3.12 mmol,

0.65 g) in dry ethanol (30 mL) at 0 °C. The reaction mixture was stirred for 16 h at rt. The reaction was cooled to 0 °C and aq HCl (1 M, 15 mL) was added carefully. The reaction mixture was extracted with diethyl ether (3×20 mL). The combined organic phases were washed with brine, dried with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by flash chromatography (ethyl acetate/hexane 1:10) and the product (*E*/*Z* 1:2.1) was obtained in 97% yield (2.95 mmol, 0.62 g) as colourless oil.

(*Z*)-*Isomer*: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.65 (1H, d, *J*=12.2 Hz, Ar–*CH*=*CH*–Ph); 6.58 (1H, d, *J*=12.2 Hz, Ar–*CH*=*CH*–Ph), 4.55 (2H, s, –*CH*$_2$OH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=63.5 (*CH*$_2$OH) ppm; Other signals of (*E*)- and (*Z*)-isomers are merged. IR (ν): 3381, 3064, 3021, 2920, 2851, 1597, 1559, 1443, 1040 cm^{-1}. HRMS: $[M-H]^+$ calcd for $C_{15}H_{13}O$: 209.0972; found: 209.0970.

3.31. (*E*)-and (*Z*)-Dimethyl 2-(2-styrylbenzyl)malonate

The title compound was prepared according to **GP3** starting from (*E*)- and (*Z*)-isomer of the corresponding alcohol (2.76 mmol, 0.58 g) in 28% yield (0.77 mmol, 0.25 g) as a colourless oil.

(*Z*)-Isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.73 (1H, d, *J*=12.2 Hz, Ar–*CH*=*CH*–Ph); 6.69 (1H, d, *J*=12.2 Hz, Ar–*CH*=*CH*–Ph), 3.70 (6H, s, COO*CH*$_3$), 3.28 (2H, d, *J*=8.0 Hz, *CH*$_2$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=32.82 (–CH_2OH), 52.5 (OCH_3), 52.6 (*C*H[COOMe]$_2$), 169.3 (C=O) ppm. Other signals of (*E*)- and (*Z*)-isomers signals are merged. IR (ν): 3060, 3024, 2952, 2847, 1754, 1735, 1495, 1436, 1276, 1229, 1151 cm^{-1}; HRMS: $[M+H]^+$ calcd for $C_{20}H_{21}O_4$: 325.1434; found: 325.1441.

3.32. Procedure for the synthesis of dimethyl 2-2(2-(3-phenyloxiran-2-yl)benzyl)malonate (6)

To a solution of compound **3a** (1.26 mmol, 428 mg) in chloroform (20 mL) *m*CPBA (1.89 mmol, 423 mg) was added. The reaction mixture was stirred at rt for 16 h. To the reaction mixture aq satd $NaHCO_3$ (2×15 mL) was added and extracted with diethyl ether (3×20 mL). The combined organic phases were washed with brine, dried with Na_2SO_4, evaporated under reduced pressure and subjected to column chromatography (ethyl acetate/hexane 1:20). The title compound was obtained in 95% yield (1.20 mmol, 410 mg) as colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ=7.42–7.36 (5H, m, Ar–*H*), 7.32–7.26 (3H, m, Ar–H), 7.21 (1H, d, *J*=7.4 Hz), 4.10 (1H, d, *J*=1.9 Hz), 3.80 (1H, d, *J*=2.0 Hz), 3.69 (1H, t, *J*=7.3 Hz), 3.64 (3H, s, COO*Me*), 3.60 (3H, s, COO*Me*), 3.32 (2H, d, *J*=7.2 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=169.1, 169.0, 136.8, 135.8, 135.5, 129.5, 128.6, 128.4, 128.0, 127.5, 125.6, 124.7, 62.2, 60.4, 52.59, 52.55, 31.4 ppm; IR (ν): 3070, 3033, 2953, 2847, 1754, 1734, 1575, 1491, 1456, 1435, 1282, 1232, 1153 cm^{-1}; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{24}O_5N$: 358.1649; found: 358.1652.

3.33. (3*S*,3a*S*,8a*R*)-Methyl 1-oxo-phenyl-3,3a,8,8a-tetrahydro-1*H*-indeno[2,1-*c*]furan-8a-carboxylate (4a′)

^{t}BuOK (0.36 mmol, 40 mg) was added to a solution of epoxide **6** (0.18 mmol, 61 mg) in *t*-BuOH (3 mL). The reaction mixture was stirred for 6 h. The reaction mixture was quenched with aq 1 M HCl (2×5 mL) and extracted with ethyl acetate (3×5 mL). The combined organic phases were washed with brine (3×5 mL), dried with Na_2SO_4 and evaporated under reduced pressure. The crude product was dissolved in MeOH (6 mL) and treated with a catalytic amount of concd H_2SO_4 in the presence of molecular sieves (4 Å). The reaction mixture was stirred at rt for 24 h. The reaction mixture was filtered. The filtrate was quenched with water (10 mL) and extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with brine (3×5 mL), dried with Na_2SO_4 and concentrated under reduced pressure. The crude was purified by flash chromatography (ethyl acetate/hexane 1:10). The title compound **4a′** was obtained as a mixture with compound **4a** (2:1) in 46% overall yield (0.082 mmol, 25 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ=6.80 (2H, m, Ar–*H*), 5.64 (1H, d, *J*=5.0 Hz), 4.64 (1H, d, *J*=5.0 Hz), 3.88 (3H, s, –$COOCH_3$) ppm; ^{13}C NMR (125 MHz, CDCl3): δ=80.6, 56.0, 53.3, 49.8, 29.0 ppm. Other signals are merged with compound **4a**. IR (ν): 3034, 2953, 2851, 1781, 1735, 1559, 1436, 1282, 1229, 1154, 1110 cm^{-1}; HRMS: $[M+H]^+$ calcd for $C_{19}H_{17}O_4$: 309.1121; found: 309.1126.

3.34. Calculations

Ab initio calculations were performed by using Gaussian 03 program (revision B.04).[35] Geometries were fully optimized at B3LYP/6-31G(d) level, and the obtained energy minimum structures were characterized by frequency calculation at the same calculation level. The energies were corrected with zero-point energies. The NMR chemical shifts were calculated at B3LYP/6-31G(d) level by the Gauge-Independent Atomic Orbital (GIAO) method[36] using an NMR keyword.

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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.2010.03.062.

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