Dimerization of conjugated 1-indanones

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Abstract: Conjugated 1-indanones dimerize under basic conditions to provide spirodimers. For example when 2-(*E*)-carbomethoxymethylene-1-indanone (**5**) was treated with Cs_2CO_3 in CH_3CN, two spirodimers, **6** and **7**, were produced via two modes of reaction (mode A and mode B). With 2-(*E*)-cyanomethylene-1-indanone (**9**) only mode A dimerized spiro products (**10** and **11**) were observed whereas with 2-chloromethylidene-1-indanone (**12**) a 1,2-dimer (**13**) was obtained instead of the expected spirodimer.

Key words: dimerization, conjugated 1-indanones, spirodimers.

Résumé : Les 1-indanones dimérisent en présence d'une base pour donner des spirodimères. Par exemple, lorsqu'on traite le 2-(*E*)-carbomethoxymethylène-1-indanone (**5**) avec Cs_2CO_3 dans CH_3CN on obtient les spirodimères **6** et **7**. Ces deux dimères sont produits par deux modes de dimérisation (mode A et mode B). Dans le cas du 2-(*E*)-cyanomethylène-1-indanone (**9**) uniquement la dimérization de type A a lieu pour produire les produits spiros **10** et **11** tandis qu'avec le 2-chloromethylidène-1-indanone (**12**) comme produit de départ on obtient un dimère de type 1,2 (**13**).

Mots clés : dimérisation, 1-indanones conjugués, spirodimères.

Introduction

In a previous report we presented our study on the dimerization of 2-benzylidene-1-indanone (**1a**, Scheme 1) (1). The structure and the stereochemistry of the major spirodimer (**3a**) obtained from this reaction had initially been established by COSY, HMQC, HMBC, and NOESY NMR correlation techniques. The structure was then confirmed by X-ray crystallography (1). The stereochemistry assigned for dimer **3a** (Scheme 1) differs from previous reports (2, 3) where X-ray crystallographic analysis was not used to prove the stereochemistry. To the best of our knowledge no examples of this dimerization other than the benzylidene case (**1a**) have been published. Herein we describe new results on the dimerization of substituted benzylidene-1-indanones and other conjugated 1-indanones to assess the generality of the reaction.

Results and discussion

For the benzylidene cases, the monomers **1b** (X = SMe) and **1c** (X = SO_2Me) were chosen as substrates to verify the effect of the electronic nature of the aromatic substituents on the outcome of the reaction. The monomer **1b** was readily prepared by condensation of 1-indanone with 4-thiomethylbenzaldehyde in EtOH under acidic conditions. The monomer **1c** derives from oxidation of **1b** with Oxone® in CH_2Cl_2–MeOH. With monomers **1b** and **1c** (Table 1), the reactions proceeded smoothly to provide the corresponding dimers (Scheme 1). Moderate yields (60%) of the spirodimers were obtained with Cs_2CO_3 as the base (entry 3 and 5, Table 1). In addition, it has been observed that in the case where KHMDS was used as the base for substrate **1b,** the reaction took place very rapidly (5 min) at –78°C to provide the corresponding spirodimers **3b** and **4b** in high yields (85%) (Table 1). The relative stereochemistry of the predominant dimers (**3b** and **3c**) is the same as that observed for the unsubstituted case (**3a**). In all cases the dimerization gave, as the major product, the spirodimers with the phenyl substituents on the convex face of the molecule.

The preceding results suggest that the electronic nature of the substituents on the aromatic ring have little influence on the outcome of the reaction. Following these results, we turned our attention to other conjugated 1-indanones without a phenyl ring. With 2-(*E*)-carbomethoxy-methylene-1-indanone (**5**) as the substrate (Scheme 2), rapid dimerization (0.5 h) was observed with Cs_2CO_3 in CH_3CN (entry 1, Table 2) providing two spirodimers, **6** and **7**, in a 1:1 ratio. The KHMDS reaction conditions (entry 2, Table 2) were also applied to indanone **5** to afford dimers **6** and **7**, also in a 1:1

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This manuscript is dedicated to Professor Hanessian to underline his major achievements in organic chemistry.
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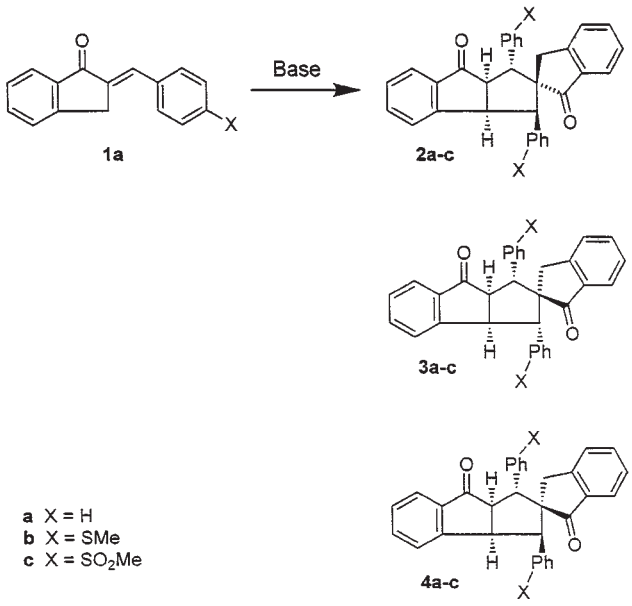
Table 1. Reaction conditions and isolated yields for the dimerization of **1a–c** to produce various spirodimers.

Entry	X	Indanone	Time	Condition	% Yield of Dimer **2**	% Yield of Dimer **3**	% Yield of Dimer **4**
1	H	**1a**	18 h	Cs_2CO_3, CH_3CN, rt	0	93	4
2	H	**1a**	5 min	KHMDS, THF, –78°C	0	81	6
3	SMe	**1b**	50 h	Cs_2CO_3, CH_3CN, rt	0	52	8
4	SMe	**1b**	5 min	KHMDS, THF, –78°C	0	80	5
5	SO_2Me	**1c**	16 h	Cs_2CO_3, CH_3CN, rt	0	57	3

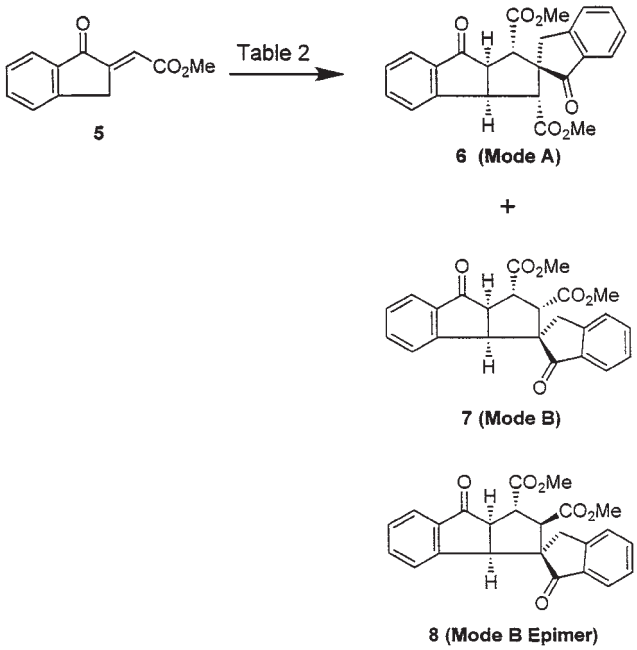
Table 2. Reaction conditions for dimerization of compound **5**.

Entry	Conditions	Yield (%)	Ratios Dimer **6**	Ratios Dimer **7**	Ratios Dimer **8**
1	Cs_2CO_3, CH_3CN, rt/30 minutes	85	1	1	—
2	KHMDS, THF, –78°C/4 minutes	80	1	1	—
3	(–)-spartine, THF, rt/18 h	83	1	2.2	—
4	DBU, THF, rt/18 h	60	3.6	2.8	1

Scheme 1.



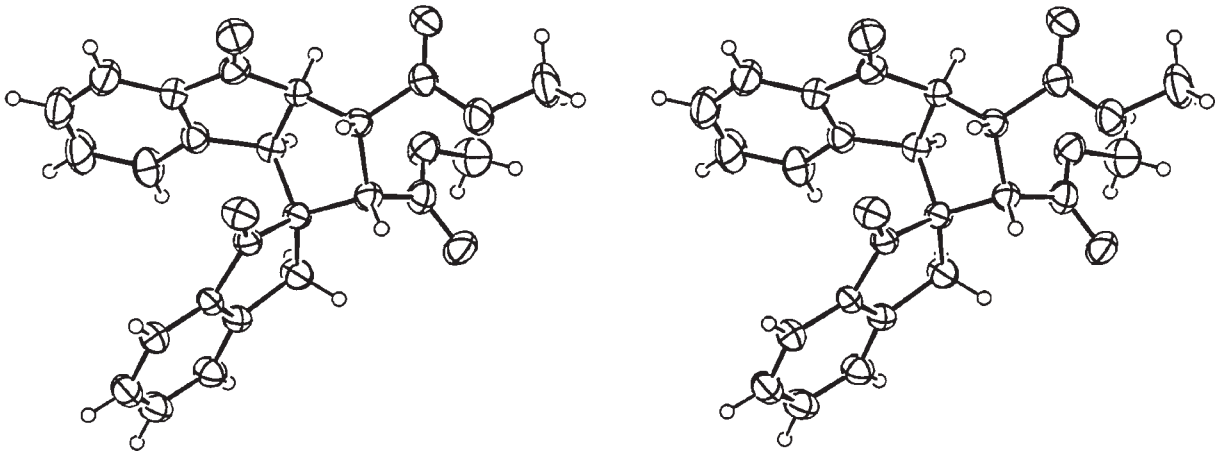
Scheme 2.



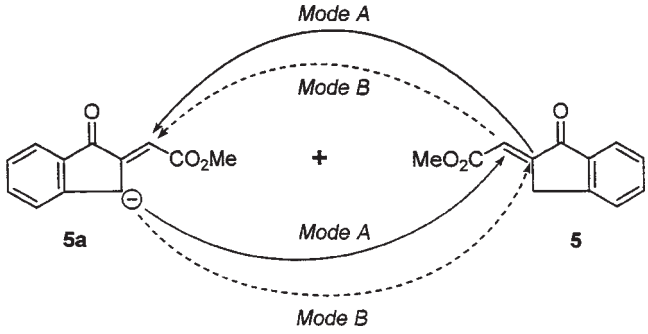
ratio. In the case where the dimerization was achieved with DBU as a base (entry 4, Table 2), a third dimer (**8**) was produced late in the reaction. This dimer is also formed from dimer **7** using DBU which suggests that compound **8** is derived by epimerization of **7**. The dimerization of **5** can also be achieved with (–)-spartine in THF to provide dimers **6** and **7** in a 1:2 ratio (entry 3, Table 2). Under these conditions no enantioselectivity was observed for this dimerization using chiral HPLC column for analysis. The spirodimers **6** and **7** are easily separable by TLC. The more mobile dimer **6** is produced by the same mode of dimerization (mode A, see Scheme 3) as observed in the benzylidene cases **1**. The second dimer originates from a different mode of dimerization (mode B) providing the vicinal diester **7**. As described in Scheme 3, the latter dimer results from the addition of the enolate **5a** onto the β carbon of the ester of a second monomer (**5**), followed by an intramolecular addition to the β carbon of the ketone. Initially, the structure and the stereochemistry of dimer **6** and of dimer **7** were established by the same NMR techniques used for the spirodimer **3a**. To prove the structure of dimer **7,** it was submitted for X-ray crystallographic analysis. As depicted in Fig. 1, the X-ray structure is identical to the structure derived from NMR.

When the dimerization of the cyano compound **9** was studied, a similar reaction pattern to that obtained with the corresponding ester **5** was expected. Using Cs_2CO_3 as a base, the dimerization of **9** was completed within a few minutes and, in contrast to ester **5**, two dimers **10** and **11** were isolated that arose from a mode A type addition. No

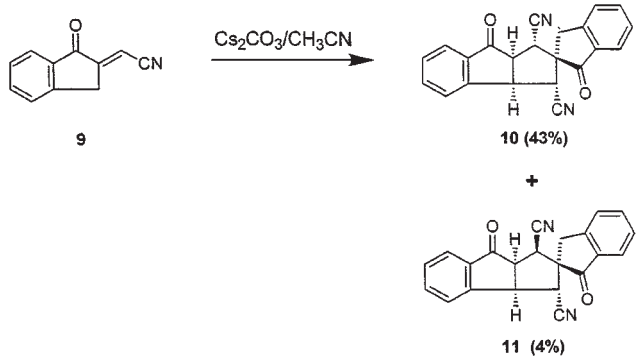
Fig. 1. Stereoview of the ORTEP representation of **7**.[3] Non-hydrogen atoms are represented by ellipsoids corresponding to 30% probability.



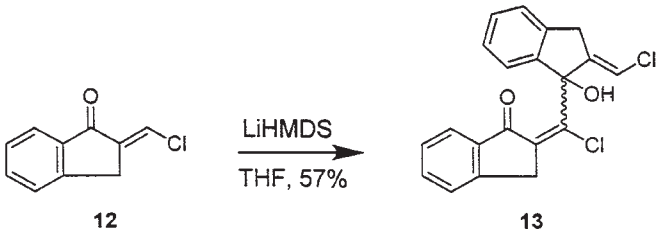
Scheme 3.



Scheme 4.



Scheme 5.



formation of a mode B type dimer was observed (Scheme 4). Presumably, the cyano compound undergoes only mode A dimerization because the addition onto the β carbon of the nitrile would lead to an intermediate with a negative charge α to the nitrile, and would thus make it less stable than in the ester case. As was the case for ester **7**, treatment of dimer **10** under basic conditions (Cs_2CO_3–CH_3CN) resulted in the production of its epimer **11**.

The last case studied was the chloromethylene analog **12** which was prepared according to a literature procedure (4). Interestingly, when this monomer was subjected to basic conditions (LiHMDS, THF, –78°C), none of the expected spirodimer was produced; however, the 1,2-dimer **13**[2] was formed exclusively (Scheme 5). It appears that the electronic nature of the substituent on the double bond has an effect on the site of reactivity of both the cross conjugated enolate and the monomer.

In conclusion, conjugated 1-indanones provide spirodimers when exposed to basic conditions. This allows the preparation of molecules containing five stereogenic centers from achiral monomers in a single step. The only exception to this statement so far is the chloromethylene analog **12**. The formation of the spirodimers is probably the result of either a double Michael reaction as already proposed (1) or of an ionic cycloaddition (Scheme 6) which could explain the high degree of diastereoselectivity observed in these reactions.

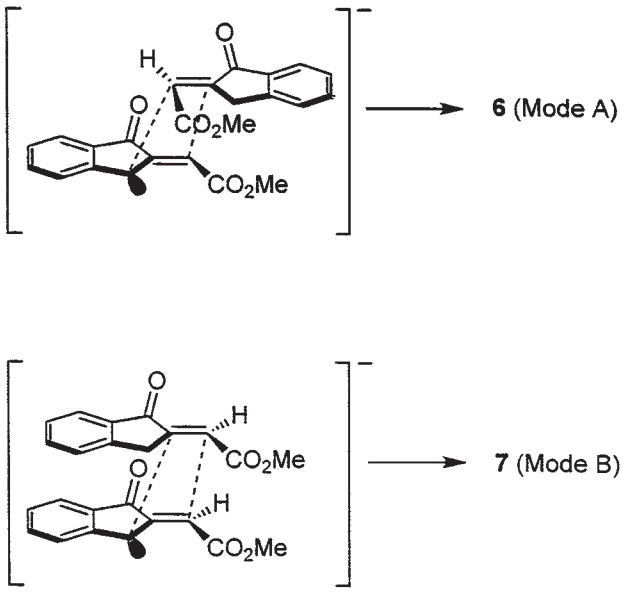
Experimental

2-(*E*)-*p*-thiomethylbenzylidene-1-indanone (1b)

To a mixture of 1-indanone (4.97 g, 37.6 mmol) and 4-thiomethylbenzaldehyde (4.60 mL, 34.6 mmol) in EtOH (50 mL) was added 25 drops of concentrated HCl. The resulting mixture was refluxed at 80°C for 19 h and then allowed to cool to room temperature to give a yellow solid. The solid was filtered and washed with EtOH to provide 8.16 g (89%) of the title compound **1b**: mp 130–133°C (EtOH); ^{1}H NMR

[2] The stereochemistry of the double bond has not been established.
[3] N.N. Tsou, R.G. Ball, C. Dufresne, and Y. Leblanc. Acta Cryst. C. (2000). In preparation.

Scheme 6.



(300 MHz, acetone-d_6, 27°C) δ: 7.79 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.69–7.66 (m, 2H), 7.52 (t, *J* = 2.1 Hz, 1H), 7.49–7.44 (m, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 4.11 (d, *J* = 2.0 Hz, 2H), 2.56 (s, 3H). ^{13}C NMR (125 MHz, acetone-d_6, 27°C) δ: 193.9, 150.7, 142.5, 138.9, 135.3, 133.2, 132.7, 132.0, 128.4, 127.4, 126.7, 124.4, 33.0, 14.8. HRMS calcd. for $C_{17}H_{15}OS$ [M + H]$^+$: 267.0842, found: 267.0843. Elemental analysis calcd. for $C_{17}H_{14}OS$: C 76.66, H 5.30, S 12.04; found: C 76.69, H 5.38, S 12.11.

2-(*E*)-*p*-methylsulfonebenzylidene-1-indanone (1c)

To a solution of **1b** (1.00 g, 3.75 mmol) in a mixture of MeOH (53 mL) and CH_2Cl_2 (5 mL) was added dropwise a suspension of OXONE® (10 g, 16.3 mmol) in water (37 mL). The resulting mixture was stirred for 28 h and then partitioned between H_2O and CH_2Cl_2. The organic phase was separated, dried over Na_2SO_4, filtered, and evaporated under reduced pressure to yield a white solid. The crude solid was stirred vigourously with Et_2O for about 5 min, filtered, and dried under vacuum for several hours to provide 0.97 g (87%) of the title compound **1c**: mp 211–214°C (EtOH); ^{1}H NMR (300 MHz, acetone-d_6, 27°C) δ: 8.06–8.04 (m, 4H), 7.83 (d, *J* = 7.8 Hz, 1H),7.75–7.68 (m, 2H), 7.62 (t, *J* = 2.3 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 4.21 (d, *J* = 2.1 Hz, 2H), 3.17 (s, 3H). ^{13}C NMR (125 MHz, acetone-d_6, 27°C) δ: 193.9, 151.0, 142.5, 141.3, 139.4, 138.4, 135.9, 132.0, 131.4, 128.7, 128.6, 127.5, 124.7, 44.2, 32.8. HRMS calcd. for $C_{17}H_{15}O_3S$ [M + H]$^+$: 299.0740, found: 299.0741.

Dimerization of 2-(*E*)-*p*-thiomethylbenzylidene-1-indanone (1b) using CS_2CO_3 as a base to yield 3b and 4b

To a stirring solution of **1b** (0.65 g, 2.00 mmol) in CH_3CN (9.5 mL) was added Cs_2CO_3 (0.65 g, 2.00 mmol). The resulting mixture was stirred for 50 h at room temperature and was then quenched by the addition of aqueous NH_4OAc (10 mL), followed by addition of ethyl acetate (50 mL). The organic phase was separated and the aqueous phase was extracted twice more with ethyl acetate (2 × 50 mL). The organic portions were combined, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The crude mixture was then purified by column chromatography with 5% EtOAc in toluene followed by a preparative plate purification (5% EtOAc in toluene) to yield 0.25 g (52%) of pure dimer **3b** and 0.040 g (8%) of isomer **4b**.

*Isomer **3b***: mp 181–183°C (EtOH); ^{1}H NMR (500 MHz, benzene-d_6, 27°C) δ: 7.78 (d, *J* = 7.1 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.01–6.91 (m, 3H), 6.89 (d, *J* = 1.6 Hz, 2H), 6.88 (d, *J* = 1.6 Hz, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.60 (app. q, 2H), 4.31 (d, *J* = 11.0 Hz, 1H), 4.06 (dd, *J* = 9.0 Hz, 1H), 3.90 (d, *J* = 11.0 Hz, 1H), 3.60 (dd, *J* = 9.0, 11.0 Hz, 1H), 2.79 (s, 2H), 1.80 (s, 3H), 1.79 (s, 3H). HRMS calcd. for $C_{34}H_{29}O_2S_2$ [M + H]$^+$: 533.1608, found: 533.1609. Elemental analysis calcd. for $C_{34}H_{28}O_2S_2$: C 76.60, H 5.30, S 12.05; found: C 76.21, H 5.34, S 12.28.

*Isomer **4b** (oil)*: ^{1}H NMR (500 MHz, benzene-d_6, 70°C) δ: 8.00 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.97 (app. s, 1H), 6.92 (t, *J* = 7.7 Hz, 1H), 6.78–6.73 (m, 3H), 6.71 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 8.3 Hz, 2H), 6.50 (d, *J* = 7.6 Hz, 1H), 4.20 (d, *J* = 4.4 Hz, 1H), 4.05 (app. t, *J* = 9.3 Hz, 1H), 3.67 (d, *J* = 10.3 Hz, 1H), 3.46 (dd, *J* = 4.2, 8.1 Hz, 1H), 2.79 (d, *J* = 17.6 Hz, 1H), 2.47 (d, *J* = 17.5 Hz, 1H), 2.07 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (125 MHz, 27°C, acetone-d_6) δ: 207.2, 205.9, 154.3, 152.5, 139.8, 139.5, 137.9, 137.8, 137.2 135.3, 134.0, 133.6, 132.2, 130.1, 129.2, 128.1, 128.0, 127.1, 126.9, 125.5, 123.9, 123.6, 68.1, 58.8, 58.7, 51.9, 49.1, 37.6, 15.2, 14.9. HRMS calcd. for $C_{34}H_{29}O_2S_2$ [M + H]$^+$: 533.1608, found: 533.1609.

Dimerization of 2-(*E*)-*p*-methylsulfonebenzylidene-1-indanone (1c) using Cs_2CO_3–CH_3CN to afford 3c and 4c

To a stirring solution of **1c** (0.10g, 0.35 mmol) in CH_3CN (1.8 mL) was added Cs_2CO_3 (0.13 g, 0.39 mmol). The resulting mixture was stirred for 16 h at room temperature and was then quenched by the addition of aqueous NH_4OAc (2 mL), followed by addition of ethyl acetate (10 mL). The organic phase was separated and the aqueous phase was extracted twice more with ethyl acetate (2 × 10 mL). The organic portions were combined, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. Addition of a 70% EtOAc in hexane solution to the crude mixture resulted in the precipitation of the major isomer **3c** as a white solid, which was filtered and dried under vacuum for several hours; to afford 0.05 g (51%). Purification of the filtrate by preparative plate (7% EtOAc–hexane) yielded a further 0.006 g of isomer **3c** (total mass obtained: 0.060 g, 57%), and 0.002 g (3%) of isomer **4c**.

*Isomer **3c***: mp 249–251°C (EtOH); ^{1}H NMR (500 MHz, benzene-d_6, 27°C) δ: 7.75 (d, *J* = 7.3 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 7.2 Hz, 1H), 6.59 (t, *J* = 7.6 Hz, 1H), 6.53 (t, *J* = 6.9 Hz, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 4.18 (d, *J* = 10.8 Hz, 1H), 3.95 (t, *J* = 9.4 Hz, 1H), 3.76 (d, *J* = 10.5 Hz, 1H), 3.47 (dd, *J* = 8.9, 10.7 Hz, 1H), 2.52 (d, *J* = 17.5 Hz, 1H), 2.47 (d,

J = 17.5 Hz, 1H), 2.10 (s, 3H), 2.07 (s, 3H). HRMS calcd. for $C_{34}H_{29}O_6S_2$ $[M + H]^+$: 597.1408, found: 597.1405. Elemental analysis calcd. for $C_{34}H_{28}O_6S_2$: C 68.44, H 4.73, S 10.75; found: C 68.42, H 4.77, S 10.81.

Isomer ***4c*** *(oil)*: ^{1}H NMR (500 MHz, benzene-d_6, 70°C) δ: 7.91 (d, J = 7.7 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 7.9 Hz, 2H), 7.34 (d, J = 8.1 Hz, 1H), 7.07 (d, J = 8.3 Hz, 2H), 6.99 (t, J = 7.6 Hz, 1H), 6.92 (t, J = 7.6 Hz, 1H), 6.87 (t, J = 7.6 Hz, 1H), 6.74 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.56 (d, J = 8.5 Hz, 2H), 6.26 (d, J = 7.8 Hz, 1H), 4.23 (d, J = 5.6 Hz, 1H), 3.96 (t, J = 9.3 Hz, 1H), 3.44 (d, J = 10.3 Hz, 1H), 3.36 (dd, J = 5.4, 8.7 Hz, 1H), 2.56 (d, J = 17.0 Hz, 1H), 2.34 (s, 3H), 2.31 (d, J = 17.0 Hz, 1H), 2.14 (s, 3H). HRMS calcd. for $C_{34}H_{29}O_6S_2$ $[M + H]^+$: 597.1408, found: 597.1405.

Dimerization of 2-(*E*)-*p*-thiomethylbenzylidene-1-indanone (1b) using $KN(SiMe_3)_2$ to yield 3b and 4b

To a solution of **1b** (0.15 g, 0.56 mmol) in THF (1.6 mL) at –78°C was added dropwise via syringe a 0.5 M toluene solution of $KN(SiMe_3)_2$ (1.2 mL, 0.60 mmol). The solution was allowed to stir for one hour at –78°C and was then quenched by addition of 3 mL of aqueous NH_4OAc via syringe followed by immediate warming to room temperature. The workup and purification procedure followed was the same as that described for the dimerization of **1b** using Cs_2CO_3–CH_3CN and yielded 0.12 g (80%) of isomer **3b** and 0.005 g (5%) of isomer **4b**.

Dimerization of 2-(*E*)-benzylidene-1-indanone (1a) using $KN(SiMe_3)_2$ to yield 3a and 4a

The experimental procedure and workup followed was that as described above for the dimerization of **1b** using $KN(SiMe_3)_2$. Quantities of reagents and solvents used: 2-(*E*)-benzylidene-1-indanone (0.10 g, 0.45 mmol); THF 1.1 mL; $KN(SiMe_3)_2$ (0.5 M, 0.92 mL, 0.460 mmol). Purification was achieved by flash column chromatography (6% EtOAc in toluene), which separated most of isomer **3a** from **4a**, followed by a preparative plate purification (6% EtOAc in toluene) to separate the remaining fractions from the previous column. This procedure yielded 0.08 g (81%) of isomer **3a** and 0.006 g (6%) of isomer **4a**. The isomers were identified on the basis of their ^{1}H NMR spectra, which were identical to those reported previously (1).

Dimerization of 2-carbomethoxymethylene-1-indanone (5) using Cs_2CO_3–CH_3CN to afford 6 and 7

To a solution of 2-carbomethoxymethylene-1-indanone (**5**) (5) (0.50 g, 2.30 mmol) in CH_3CN (22 mL) was added Cs_2CO_3 (0.75 g, 2.30 mmol). The resulting mixture was stirred at room temperature for 0.5 h. The reaction mixture was partitioned between 25% aqueous NH_4OAc and ethyl acetate. The organic phase was separated, dried over Na_2SO_4, and evaporated. The crude mixture was purified by flash chromatography to afford dimer **6** (0.19 g, 43%) and dimer **7** (0.19 g, 42%).

Dimer ***6***: mp 163–164°C. ^{1}H NMR (500 MHz, benzene-d_6, 22°C) δ: 7.79 (d, J = 7.7 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.3 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.92 (t, J = 7.3 Hz, 1H), 6.84 (t, J = 7.3 Hz, 1H), 4.16 (t, J = 9.9 Hz, 1H), 3.78 (t, J = 9.4 Hz, 1H), 3.67 (d, J = 9.5 Hz, 1H), 3.30 (d, J = 10.1 Hz, 1H), 3.07 (d, J = 17.6 Hz, 1H), 2.83 (s, 3H), 2.79 (s, 3H), 2.77 (d, J = 16.6 Hz, 1H). ^{13}C NMR (125.6 MHz, acetone-d_6, 22°C) δ: 203.8, 202.0, 171.0, 170.4, 154.5, 151.0, 137.0, 136.0, 135.0, 127.7, 127.6, 126.3, 126.0, 124.6, 124.4, 124.1, 63.4, 58.0, 53.5, 52.1, 51.1, 51.0, 45.0, 32.4. Elemental analysis calcd. for $C_{24}H_{20}O_6$: C 71.28, H 4.98; found: C 71.30, H 4.87. Mass spectrum m/z = 405.

Dimer ***7***: mp 170–171°C ^{1}H NMR (500 MHz, benzene-d_6, 22°C) δ: 7.68 (d, J = 6.7 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H), 6.99 (d, J = 7.4 Hz, 1H), 6.82 (m, 3H), 6.48 (d, J = 7.4 Hz, 1H), 4.30 (dd, J = 4.4, 7.3 Hz, 1H), 3.77 (dd, J = 4.4, 7.9 Hz, 1H), 3.70 (d, J = 7.9 Hz, 1H), 3.63 (d, J = 17.0 Hz, 1H), 3.46 (d, J = 7.4 Hz, 1H), 3.35 (s, 3H), 3.22 (s, 3H), 2.97 (d, J = 17.0 Hz, 1H). ^{13}C NMR (125.6 MHz, acetone-d_6), 298 K) δ: 204.7, 204.7, 173.0, 171.3, 151.7, 151.2, 137.7, 136.7, 134.8, 133.9, 127.0, 127.2, 126.6, 126.3, 124.2, 123.8, 60.4, 55.3, 55.2, 53.9, 51.9, 51.2, 47.7, 39.3. Elemental analysis calcd. for $C_{24}H_{20}O_6$: C 71.28, H 4.98; found: C 71.26, H 5.08. Mass spectrum m/z = 405.

Dimerization of 2-carbomethoxymethylene-1-indanones (5) using $KN(SiMe_3)_2$ to yield 6 and 7

The indanone **5** (0.05 g, 0.25 mmol) was dissolved in THF (1.5 mL) and cooled to –78°C for 5 min. This was followed by the addition of a 0.05 M solution of $KN(SiMe_3)_2$ in toluene (0.10 eq, 50 μL). The crude deep purple mixture was partitioned between ethyl acetate and 25% aqueous NH_4OAc. The organic layer was separated, dried over $MgSO_4$, and filtered through silica gel to provide the title products **6** and **7** (0.04 g, 80% yield) in a 1:1 ratio.

Dimerization of 2-carbomethoxymethylene-1-indanones (5) using DBU to yield 6,7 and 8

To a solution of the indanone **5** (0.25 g, 1.24 mmol) in THF (5 mL) was added DBU (0.18 mL, 6.20 mmol). The resulting dark purple solution was allowed to react overnight and this resulted in an additional dimeric product that was more polar than those seen previously (**6** and **7**). The mixture of dimers was purified to afford: 0.07 g (28.4%) of **6**, 0.06 g (22.4%) of **7** and 0.008 g (8.0%) of **8**: Dimer **8** mp 198–200°C. ^{1}H NMR (500 MHz, acetone-d_6, 22°C) δ: 7.66 (t, J = 7.3 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.56 (d, J = 7.3 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 7.1 Hz, 1H), 6.91 (d, J = 7.5 Hz, 1H), 4.43 (d, J = 8.7 Hz, 1H), 4.02 (dd, J = 6.0, 11.5 Hz, 1H), 3.98 (d, J = 11.5 Hz, 1H), 3.89 (d, J = 17.5 Hz, 1H), 3.82 (d, J = 17.5 Hz, 1H), 3.77 (s, 3H), 3.50 (dd, J = 6.2, 9.0 Hz, 1H), 3.35 (s, 3H). ^{13}C NMR (125.6 MHz, acetone-d_6, 22°C) δ: 206.4, 206.1, 175.2, 171.4, 153.5, 150.8, 138.4, 138.1, 135.9, 134.9, 129.3, 128.3, 127.2, 126.5, 124.0, 123.8, 60.1, 59.4, 55.8, 54.3, 52.6, 52.1, 46.5, 40.1. HRMS calcd. for $C_{24}H_{21}O_6$ $[M + H]^+$: 405.1339, found: 405.1338.

Preparation of spirodimer 8 from dimer 7

To a solution of dimer **7** (0.02 g, 0.04 mmol) in THF (0.40 mL) was added DBU (0.06 mL, 0.39 mmol). After a

period of 72 h at room temperature, the reaction mixture was partitioned between ethyl acetate and 25% aqueous NH_4OAc. The organic layer was separated, dried over Na_2SO_4, filtered, and evaporated. After purification by flash chromatography, dimer **8** was obtained (0.012 g, 75%).

Preparation of 2-(1-oxo-1,3-dihydro-2*H*-inden-2-ylidene)acetonitrile (9)

To a mixture of 2-carboxymethylene-1-indanone (6) (0.50 g, 2.66 mmol) in dichloromethane (5.0 mL) was added an excess of oxalyl chloride (1.0 mL, 11.5 mmol) and a catalytic amount of dry DMF. This resulting mixture was allowed to react for 1.5 h at room temperature. At this point, the solvent was evaporated in vacuo and the excess of oxalyl chloride co-evaporated with dichloromethane (3 × 5 mL). The acid chloride was then dissolved in THF (10 mL) and added to a cold solution of saturated NH_4OAc (50 mL). The ice cooled reaction mixture was then stirred for 30 min. The aqueous phase was extracted with ethyl acetate and the organic layer was dried over $MgSO_4$, filtered, and the solvent evaporated under reduced pressure to provide 0.38 g (77%) of a white solid. The acetamide was used to synthesize the nitrile without further purification. To a 0°C solution of the acetamide (0.16 g, 0.85 mmol) and pyridine (0.13 g, 1.70 mmol) in 1,4-dioxane was then added trifluoroacetic anhydride (0.19 g, 0.94 mmol) over a period of 1 hour. The slurry was kept at 0°C during the addition of the trifluoroacetic anhydride. The reaction was stirred for an additional 5 min and was then poured onto a cold NH_4OAc buffer solution. The aqueous layer was extracted with ethyl acetate, dried over $MgSO_4$, and the solvent evaporated in vacuo to provide a crude brown solid. The compound was purified by flash chromatography (20% ethyl acetate – hexanes) to provide **9** as a white crystalline material (0.10 g, 69%), mp 138–140°C. ^{1}H NMR (500 MHz, acetone-d_6, 22°C) δ: 7.83 (d, J = 7.8 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 6.50 (t, J = 2.5 Hz, 1H), 4.10 (d, J = 2.3 Hz, 2H).^{13}C NMR (500 MHz, acetone-d_6, 295 K) δ: 190.5, 156.6, 149.6, 137.5, 136.8, 129.0, 127.2, 124.8, 116.5, 101.0, 32.0. calcd. for $C_{11}H_7NO$: C 78.09, H 4.17, N 8.28; found: C 78.18, H 4.02, N 8.19. Mass spectrum m/z = 168 (M – 1).

Dimerization of 2-(1-oxo-1,3-dihydro-2*H*-inden-2-ylidene)acetonitrile (9) with Cs_2CO_3–CH_3CN to yield 10 and 11

To a solution of the nitrile **9** (0.14 g, 0.89 mmol) in acetonitrile (8 mL) was added Cs_2CO_3 (0.75 g, 2.30 mmol). After a period of 10 min, followed by standard work up procedure, the crude mixture was purified on silica gel using flash chromatography (40% ethyl acetate – hexanes followed by 60% ethyl acetate – hexanes for the more polar compound). This afforded one major dimer **10** (0.06 g, 43%) mp >230°C and a minor dimer **11** (0.006 g, 4%) mp >230°C.

*Dimer **10***: ^{1}H NMR (500 MHz, chloroform-d_3, 22°C) δ: 7.86 (d, J = 7.8 Hz, 2H), 7.79 (t, J = 7.4 Hz, 1H), 7.78 (t, J = 6.8 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 4.35 (t, J = 9.7 Hz, 1H), 3.69 (d, J = 17.5 Hz, 1H), 3.67 (t, J = 8.8 Hz, 1H), 3.65 (d, J = 17.5 Hz, 1H), 3.35 (d, J = 9.2 Hz, 1H), 3.07 (d, J = 10.1 Hz, 1H). ^{13}C NMR (125.6 MHz, acetone-d_6, 22°C) δ: 201.9, 200.9, 153.0, 152.5, 137.9, 137.1, 136.4, 135.6, 130.5, 129.6, 128.0, 126.6, 125.3, 125.3, 117.9, 117.8, 64.5, 54.2, 48.1, 42.4, 37.8, 34.7. Calcd. for $C_{22}H_{14}N_2O_2$: C 78.09, H 4.17, N 8.28; found: C 77.87, H 4.21, N 8.02. Mass spectrum m/z = 339 $(M - H)^-$.

*Dimer **11***: ^{1}H NMR (500 MHz, chloroform-d_3, 22°C) δ: 7.90 (d, J = 7.7 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.79 (t, J = 7.6 Hz, 1H), 7.75 (t, J = 7.9 Hz, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 7.7 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 4.37 (t, J = 8.7 Hz, 1H), 3.77 (t, J = 9.8 Hz, 1H), 3.74 (d, J = 17.1 Hz, 1H), 3.62 (d, J = 8.7 Hz, 1H), 3.40 (d, J = 9.2 Hz, 1H), 3.25 (d, J = 17.3 Hz, 1H). ^{13}C NMR (125.6 MHz, CD_3CN, 22°C) δ: 202.6, 201.3, 153.7, 152.4, 137.9, 137.6, 135.7, 130.7, 129.8, 128.0, 127.2, 125.4, 125.1, 119.1, 117.8, 118.6, 63.6, 53.8, 48.4, 41.6, 39.6, 37.9. HRMS calcd. for $C_{22}H_{14}N_2O_2$ $[M + H]^+$: 339.1332, found: 339.1333.

Preparation of spirodimer 11 from dimer 10

To a solution of the dimer **10** (0.02 g, 0.06 mmol) in THF (0.40 mL) was added DBU (0.03 mL, 0.19 mmol). After a period of 72 h at room temperature, the reaction mixture was partitioned between EtOAc and saturated NH_4OAc. The organic layer was separated, dried over Na_2SO_4, filtered, and evaporated. After purification by flash chromatography, dimer **11** was obtained (0.006 g, 30%), with no trace of **10** in the reaction.

Dimerization of 2-chloromethylidene-1-indanone (12) using LiHMDS to yield 13

To a solution of 2-chloromethylidene-1-indanone (**12**) (4) (0.15 g, 0.84 mmol) in THF (4 mL) at –78°C was added LiHMDS 500 μL of 1.0 M solution in THF, 0.50 mmol). After a period of 5 min, followed by standard workup procedure, the crude mixture was purified by flash chromatography (20% ethyl acetate – hexanes). White crystalline, air sensitive material was isolated in 57% yield (0.08 g). Compound **13** mp 90–110°C (decomposes). ^{1}H NMR (500 MHz, acetone-d_6, 22°C) δ: 8.66 (s, 1H), 7.88 (d, J = 7.5 Hz, 1H), 7.80 (td, J = 7.5, 0.9 Hz, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.56 (td, J = 7.2, 0.7 Hz, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.39 (dd, J = 6.9, 0.5 Hz, 1H), 7.36 (td, J = 7.1, 1.0 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.71 (t, J = 2.7 Hz, 1H), 4.03 (d, J = 21.1 Hz, 1H), 3.98 (d, J = 21.1 Hz, 1H), 3.89 (dd, J = 21.1, 2.2 Hz, 1H), 3.79 (dd, J = 21.1, 2.2 Hz, 1H). ^{13}C NMR (125.6 MHz, acetone-d_6, 22°C) δ: 194.1, 155.8, 150.8, 150.5, 149.5, 147.1, 140.3, 139.7, 137.3, 135.8, 130.3, 129.1, 128.5, 127.2, 125.8, 125.2, 118.5, 89.6, 37.5, 36.6. HRMS calcd. for $C_{20}H_{15}Cl_2O_2$ $[M + H]^+$: 357.0448, found: 357.0449.

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