Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c4ob01977f

A domino reaction of tetrahalo-7,7-dimethoxybicyclo[2.2.1]heptenyl alcohols leading to indenones and a *de novo* synthesis of ninhydrin derivatives†

Kaki Raveendra Babu and Faiz Ahmed Khan*

Received 17th September 2014,
Accepted 22nd October 2014

DOI: 10.1039/c4ob01977f

www.rsc.org/obc

An efficient acid induced rearrangement of a tetrahalo-7,7-dimethoxybicyclo[2.2.1]heptenyl system leading to substituted indenones is reported. This domino reaction involves dehydration, olefin isomerization, ketal hydrolysis, [3,3]-sigmatropic rearrangement and dehydrohalogenation. The resultant vicinal dihalo olefin moiety in the efficiently generated indenone derivatives was utilized to transform into ninhydrin derivatives by employing Ru(III)-catalyzed oxidation.

Introduction

In the recent past, the development of new synthetic routes involving one pot transformation has been an attractive area of research in organic synthesis. Among these, domino[1] reactions play an important role, because of their ability to build new scaffolds in a single step. The indenone core is an important structural motif in several natural products of biological importance.[2] For example, a structural analogue of indenone **1** is used as a fluorescent binding agent to estrogen receptors,[3] neo-lignin[4] **2** was isolated from Virolasebifera plant fruits, and compound **3** is a structural analogue of the selective COX-2 inhibitor nimesulide.[5] Indenones were used as intermediates in the synthesis of fluorenones[6] (**4**), which are important structural motifs in various natural products, and alcyopterosin N[7] contains an indanone core (Fig. 1).

Additionally, indenone derivatives are used as fermentation activators,[8] estrogen binding receptors,[9] and precursors for C-nor-D-homo-steroids,[10] gibberellins,[11] liquid crystals such as indenes,[12] indanones,[13] 2,4- and 3,4-disubstituted 1-naphthols[14] and photochromic indenone oxides.[15] On account of their importance, various methods have been developed to synthesize indenone derivatives, for example conventional organic synthetic methods such as Friedel–Crafts,[16] Grignard[17] and transition metal-mediated (rhodium,[18a–c] cobalt[18d] and ruthenium[18e]) reactions of alkynes and palladium catalysed coupling methods.[18f–h] It is worth mentioning that phenyl derivatives invariably serve as the precursors for indenones in most of the literature reports.

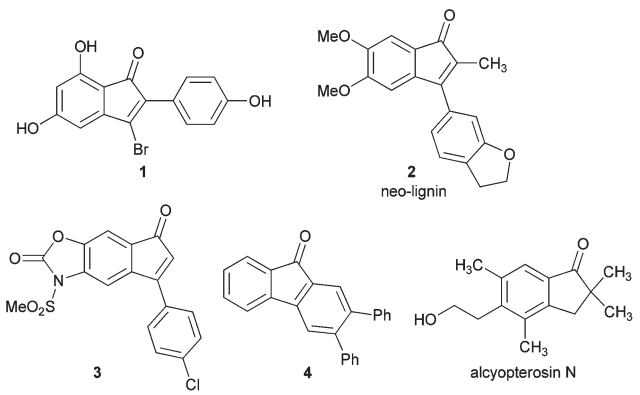


Fig. 1 Compounds containing indenone cores.

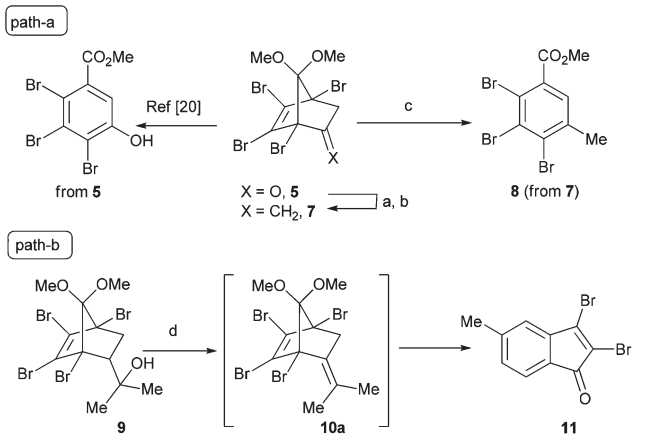
Results and discussion

Tetrahalobicyclo[2.2.1]heptenyl derivatives[19] are readily available substrates through the Diels–Alder reaction, and are extensively used as convenient templates in organic syntheses, particularly natural products. As represented in Table 1, during the last decade we have reported the Grob-type fragmentation reaction of **5** leading to 2,3,4-trihalophenol derivatives.[20] We thought that this methodology could be extended to prepare alkylated benzene derivatives from the corresponding exocyclic olefins through the same mechanistic pathway. The parent olefin **7**, which was not attainable through a simple Wittig reaction, perhaps due to the enolizable nature of the ketone,[20] was prepared *via* a methyl

Department of Chemistry, Indian Institute of Technology Hyderabad, Ordnance Factory Estate, Yeddumailaram-502205, India. E-mail: faiz@iith.ac.in

†Electronic supplementary information (ESI) available. CCDC 1015482. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ob01977f

Table 1 Initial approach for synthesis of alkylated 2,3,4-trihalobenzene derivative **8** *via* Grob-type Fragmentation (path-a) and unexpected formation of indenone **11** (path-b)[a]



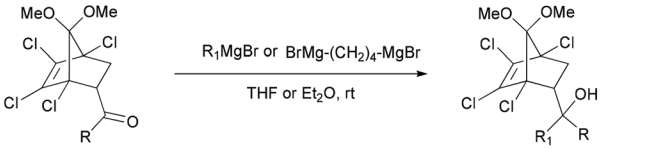
[a] Reagents and conditions: (a) MeMgI, Et_2O, rt, 1 h, 91%, (b) $SOCl_2$, pyridine, 0° C–rt, 5 h, 60%, (c) *p*-TsOH, toluene, reflux, 17 h, 84%, (d) *p*-TsOH, toluene, reflux, 23 h, 94%.

Grignard addition, followed by elimination. As expected, subjecting **7** to *p*-toluenesulfonic acid (PTSA) gave **8** in good yield. Based on the premise that tertiary alcohol **9**[21] under PTSA conditions would also yield the corresponding alkylated benzene derivative through exocyclic olefin **10a**, an experiment was carried out and the results are represented in Table 1. To our surprise, the compound **9** underwent a domino reaction *via* Cope rearrangement[22] to deliver indenone **11** in excellent yield. It worth mentioning that 4,5,6,7-tetrachloro-3a,4,7,7a-tetrahydro-4,7-methanoinden-8-one was reported to undergo smooth Cope rearrangement rather than the anticipated CO extrusion reaction for these systems.[23] Here, we wish to report this serendipitously observed, efficient acid-induced domino reaction of tetrahalo-7,7-dimethoxybicyclo[2.2.1]heptenyl alcohols leading to indenones. Furthermore, conversion of these indenones to ninhydrins, by employing Ru(III)-catalyzed oxidation, is also discussed. This, to the best our knowledge, represents a *de novo* synthesis.

Initially, the Diels–Alder adducts of methyl acrylate and vinyl ketones **12** and **13**[24] obtained from 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene have been utilized to prepare alcohols **14a–d**[21] (yield 91–99%) and **15a–l** (yield 92–99%), respectively, by treatment with Grignard reagents, as represented in Table 2. After preparing various alcohols, we turned our attention to executing the domino reaction as observed for **9**. In the beginning, tertiary alcohols with two similar alkyl substituents (**9**, **14a–c**) were treated with PTSA in refluxing toluene (23–60 h). As depicted in Table 3, indenones (**11**, **16a–c**) were obtained in good yields (71–9 4%). Notably, in addition to the alkyl substituted alcohols, the cyclopentanol **14d** delivered tricyclic cyclopentanulated indenone **16d** in good yield.

In order to determine the regioselectivity of this transformation, we became interested in probing the reaction of alcohols

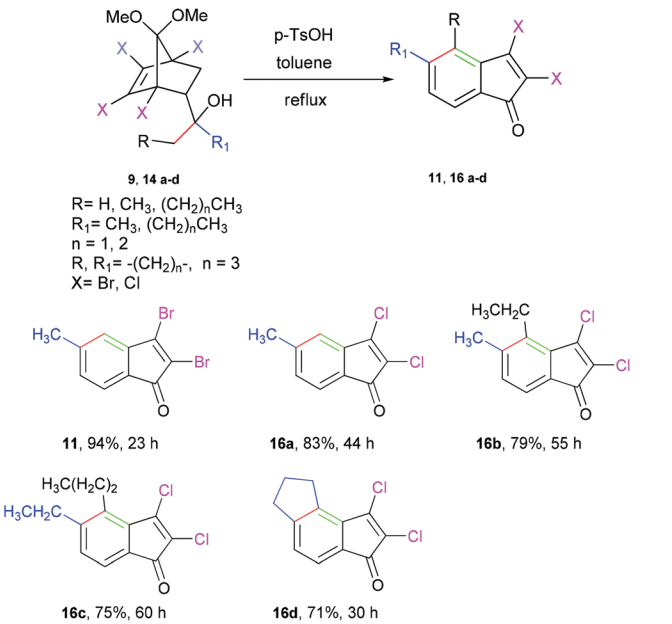
Table 2 Synthesis of tertiary alcohols (**14a–d** and **15a–l**) from **12** and **13**



Entry	Product	R, R_1	Time (h)	Yield[a] (%)
1	**14a**	R, R_1 = $-CH_3$	3.5	89
2	**14b**	R, R_1 = $-CH_2-CH_3$	4	89
3	**14c**	R, R_1 = $-(CH_2)_2CH_3$	5	99
4	**14d**	R, R_1 = $-(CH_2)_4-$	6	91
5	**15a**	R = $-CH_3$, R_1 = $-CH_2-CH_3$	5	99
6	**15b**	R = $-CH_3$, R_1 = $-(CH_2)_2CH_3$	9	98
7	**15c**	R = $-CH_3$, R_1 = $-(CH_2)_3CH_3$	9	94
8	**15d**	R = $-CH_3$, R_1 = $-(CH_2)_4CH_3$	13	99
9	**15e**	R = $-CH_3$, R_1 = $-(CH_2)_5CH_3$	13	97
10	**15f**	R = $-CH_3$, R_1 = $-(CH_2)_7CH_3$	16	99
11	**15g**	R = $-CH_3$, R_1 = $-(CH_2)_{11}CH_3$	6	98
12	**15h**	R = $-CH_3$, R_1 = $-CH_2-C_6H_5$	10	98
13	**15i**	R = $-CH_3$, R_1 = $-C_6H_5$	8	99
14	**15j**	R = $-CH_3$, R_1 = *p*-$CH_3-C_6H_4-$	15	98
15	**15k**	R = $-CH_3$, R_1 = *o*-$OMe-C_6H_4-$	14	92
16	**15l**	R = $-CH_3$, R_1 = *m*-$CH_3-C_6H_4-$	13	99

[a] Yields refers to isolated yields of chromatographically pure products. For compound **14a** see ref. 21.

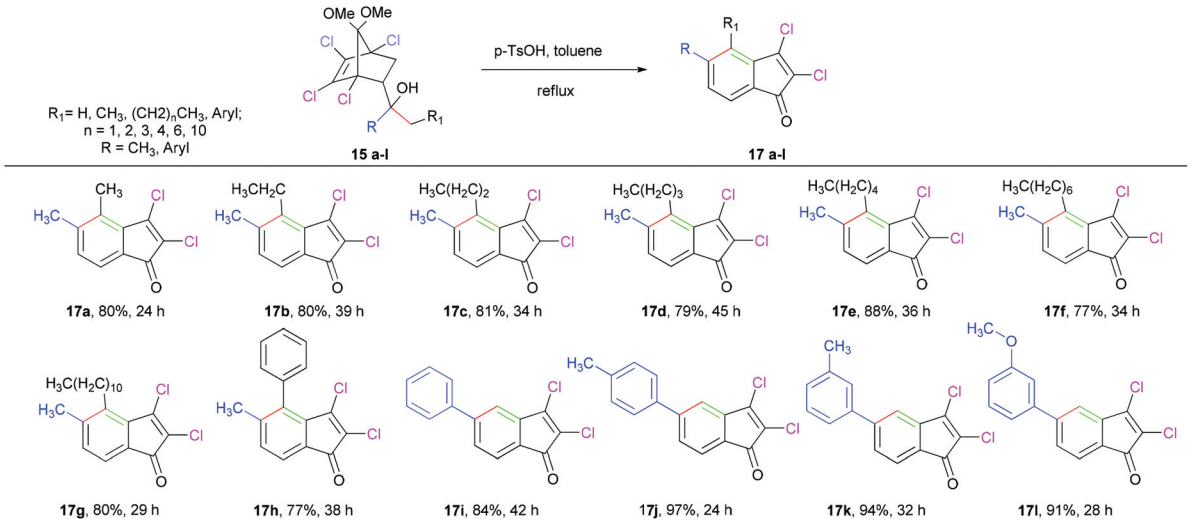
Table 3 Acid mediated one pot synthesis of 2,3-dihaloindenones *via* [3,3]-sigmatropic rearrangement[a]



[a] All reactions were carried out using 5 equiv. *p*-TsOH. Yields referreds to isolated yields of chromatographically pure products.

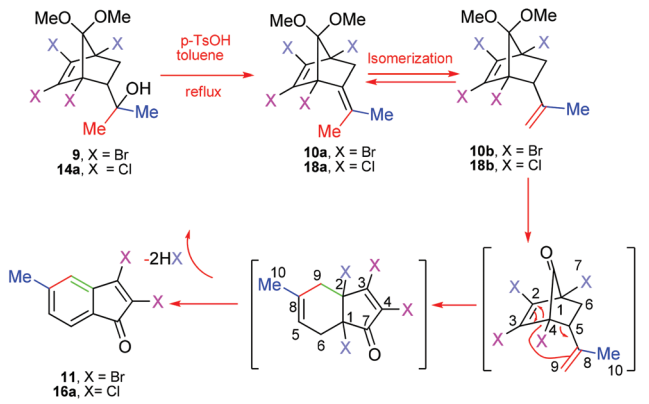
15a–l, and the results are summarized in Table 4. However, the presence of two different groups (R and $-CH_2R^1$) in this case is expected to give two regioisomers, surprisingly in all cases

Table 4 Regioselective transformation of alcohols **15a–l** *via* [3,3]-sigmatropic rearrangement[a]



[a] All reactions were carried out by using 5 equiv. *p*-TsOH. Yields refers to isolated yields of chromatographically pure products.

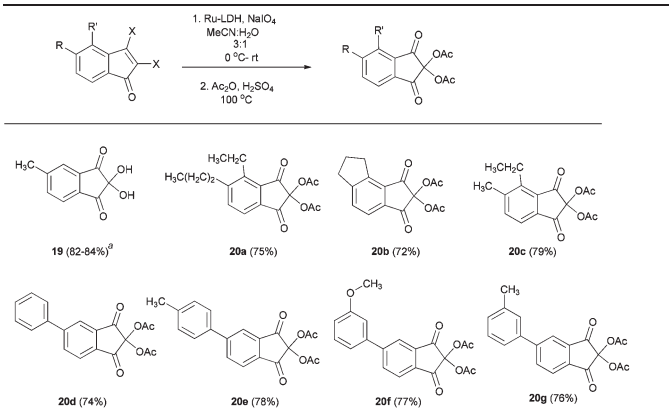
isolated indenones (**17a–l**) as single regioisomers. The high regioselectivity leading toa single indenone may be attributed to the preferential formation of a more substituted alkene upon dehydration and isomerization of the initially formed exocyclic alkene. A plausible mechanism for formation of indenones (**11**, **16a**) from alcohols (**9**, **14a**) is depicted in Scheme 1. Under acidic conditions, the tertiary alcohols are expected to undergo dehydration to give a mixture of two interconvertible isomeric olefins (**10a,b** and **18a,b**). This was confirmed by intercepting the reaction after 15 minutes and characterizing the inseparable mixture of isomeric olefins (**10a,b** and **18a,b**) using ^{1}H, ^{13}C NMR (see ESI†). At this stage, refluxing the mixture of olefins (**10a,b** or **18a,b**), thus intercepted, in xylene in the absence of PTSA did not afford the indenone. Evidently, PTSA plays a further role after dehydration to transform the ketal moiety into the carbonyl group. The resulting ketone would then furnish the fused bicycle *via* rearrangement,[23] as detailed in Scheme 1. Finally, dehydrohalogenation of fused bicyclic intermediates leads to indenones (**11**, **16a**).



Scheme 1 A plausible mechanism for the formation of indenone.

Having various substituted indenone derivatives with vicinal dihalo olefin functionality, we wanted to prepare ninhydrin derivatives by Ru(III) catalyzed oxidation.[25] The use of ninhydrins received significant attention from many research groups globally, due to their wide ranging applications, which includes analysis and detection of amino acids, proteins, agricultural, analytical and forensic sciences, and especially for the detection of latent fingerprints.[26] We anticipated that the synthesized vicinal halo indenones are the best precursors for the synthesis of ninhydrin derivatives due to the existence of a facile method for the conversion of vicinal dihalo alkene to the α-diketone moiety.[25] The details of preparation of various ninhydrin derivatives (**19**, **20a–g**) from indenones (**11**, **16a–b,d** and **17b,i–l**) are tabulated in Table 5. Apart from compound **19**[27]

Table 5 Ru(III) catalyzed oxidation of compounds **11**, **16a–b,d** and **17b,i–l**



[a] Compound **19** was isolated after Ru-LDH oxidation, from **11** yield 84% and from **16a** yield 82%. Yields refers to the isolated two-step, overall yield, apart from compound **19**.

all the ninhydrin derivatives obtained after oxidation of substrates (**16b,d**, **17b** and **17i–l**) were characterized by converting them into the corresponding diacetate derivatives (**20a–g**).

Conclusions

In conclusion, we have demonstrated an unprecedented domino reaction for the formation of indenone derivatives, and an efficient synthesis of indenones starting from unconventional (non-aromatic) precursors is described. The methodology allows facile incorporation of two different types of substituents (alkyl and aryl) at the 4 and 5 positions (indenone numbering) of indenones. The two halogens that are present on the same side as the *endo*-substituent (shown in pink) are retained in the final structure and could serve as convenient handles for further elaboration. A plausible mechanistic pathway has been discussed. The indenones with vicinal dihalo alkene moiety were converted to ninhydrin derivatives in good yields using cat. Ru-LDH and $NaIO_4$ as the co-oxidant.

Experimental section

General

All reactions were performed in oven dried apparatus. Commercial grade solvents were distilled before use. Melting points were obtained in open capillary tubes and are uncorrected. Infrared spectra were recorded as neat. The samples for NMR were made by dissolving in $CDCl_3$ and TMS is used as an internal standard; the δ values for the peaks in ^1H NMR were reported in terms of ppm with reference to TMS (0 ppm) peak and the coupling constants were reported in Hz. The multiplicities are reported as follows br = broad, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, quin = quintet, sxt = sextet, m = multiplet. The chemical shift in ^{13}C NMR is assigned by fixing the middle peak of $CDCl_3$ at 77.00 ppm. HRMS was recorded using electron spray ionization (ESI) or atmospheric chemical ionization (APCI) mode. The reactions were monitored by thin layer chromatography (tlc) on microscopic slides coated with silica gel and visualization of the spots was accomplished by exposure to iodine vapor or spraying with 4% ethanolic H_2SO_4 solution or by UV radiation. The silica gel (100 × 200) column chromatography was carried for purification of compounds with various combinations of hexane and EtOAc solvent system as the eluent. Diethyl ether and tetrahydrofuran were distilled immediately prior to use from sodium/benzophenoneketyl under argon. Distilled water was used for the reactions. LDH refers to Layered Double Hydroxide.

General procedure for compounds 6, 14b–d, 15a–l (synthesis of tertiary alcohols)

A diethyl ether or tetrahydrofuran solution of alkyl or aryl magnesium halide was prepared from Mg turnings (4 mmol), a catalytic amount of iodine ≈5 mg, and alkyl or aryl halide (5 mmol) in 5 mL dry diethyl ether or THF as per standard procedures. After the metal was completely consumed, the substrate (1 mmol) in 3 mL ether or THF was added slowly under an argon atmosphere. The reaction mixture was stirred for a specified time at room temperature (completion of the starting material as per tlc), cooled, and quenched with saturated NH_4Cl solution (1 mL). The reaction mixture was extracted thrice with ethyl acetate (3 × 10 mL). The combined organic layer was washed once with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude reaction mixture was purified by chromatography using silica gel.

General procedure for the preparation of indenone derivatives (11, 16a–d, 17a–l) and compound 8 (synthesis of indenones)

p-Toluenesulfonic acid monohydrate (2 mmol), was added to a solution of the bicyclic alcohols (0.388 mmol) in toluene (6 mL) and the reaction mixture was refluxed for specified time. After the reaction was complete (tlc monitoring), the reaction mixture was diluted with water (2 mL) and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography.

General procedure for compounds 10a, 10b, 18a and 18b

p-Toluenesulfonic acid monohydrate (0.151 mmol), was added to a solution of the bicyclic alcohol (0.076 mmol) in toluene (1 mL) and the reaction mixture was refluxed for 15 min. After the reaction was complete (tlc monitoring), the reaction mixture was diluted with water (2 mL) and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (2 mL) and dried over anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure to furnish a residue, which was purified by silica gel column chromatography.

General procedure for ninhydrin derivatives 20a–g (synthesis of ninhydrins)

To a stirred solution of indenones (0.418 mmol) in acetonitrile (3 mL) at 0 °C was added a solution of Ru-LDH (20, mg 0.83 mol% $RuCl_3$ loaded on LDH) and $NaIO_4$ (1.0455 mmol) in water (1 mL). The mixture was stirred for 5 h at −10 to 0 °C, after completion of the reaction (monitored by TLC). The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (10 mL). Concentration of the filtrate, and followed by silica gel column chromatography of the obtained residue, afforded a viscous liquid. Then the liquid was treated with acetic anhydride (1 mL) and a catalytic amount of concentrated (98%) sulfuric acid was added. The reaction mixture was stirred for 15 min at room temperature and was heated at 100 °C. Then the reaction mixture was cooled in an ice bath and diluted with water (0.5 mL). The solution was extracted with ethyl acetate (3 × 5 mL), washed with saturated $NaHCO_3$ solution (2 mL) and

dried over anhydrous Na_2SO_4. The solvent was then concentrated under reduced pressure to yield a residue, which was purified by silica gel column chromatography.

1,4,5,6-Tetrabromo-7,7-dimethoxy-2-methylbicyclo[2.2.1]-hept-5-en-2-ol (6). Yield 91%, R_f = 0.4 (15% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 1H), 3.69 (s, 3H), 3.60 (s, 3H), 2.33 (d, 1H, J = 12.8 Hz), 2.16 (d, 1H, J = 12.5 Hz), 1.12 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.8, 125.0, 113.1, 80.2, 68.0, 53.4, 51.9, 49.4, 23.5; IR ν_{max} (neat) 3521, 2986, 2948, 2843, 1573, 1445, 1393, 1361, 1264, 1214, 1184, 1101, 978, 928, 852, 827, 718, 663 cm^{-1}; HRMS (ESI) m/z calcd for $C_{10}H_{12}Br_4NaO_3$ $[M + Na]^+$ 522.7376; found 522.7368.

Preparation of exocyclic double bond containing compound (7). To a solution of compound **6**, 217 mg (0.434 mmol) in 1.5 mL anhydrous pyridine cooled to −10 °C was treated for 1 min with 1 mL of a 1 : 1 mixture of thionyl chloride and anhydrous pyridine. The reaction was stirred at −10 °C to rt for 5 h and was poured into 50 mL cold pentane. The pentane solution was treated cautiously with ice chips and the resulting layers separated. Several pentane extracts were combined and washed with two portions of 3% aqueous hydrochloric acid, followed by brine until neutral. The pentane extract was dried with anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure to yield a residue, which was purified by silica gel column chromatography to afford colorless solid **7**, yield 60% (125 mg, 0.259 mmol), R_f = 0.64 (5% EtOAc in hexane, silica gel tlc), mp 69–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (s, 1H) 5.08 (s, 1H), 3.63 (s, 3H), 3.58 (s, 3H), 2.99 (d, 1H, J = 14.5 Hz), 2.6 (d, 1H, J = 18.5 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 143.7, 127.1, 125.2, 111.6, 109.5, 67.7, 53.0, 51.9, 42.7; IR ν_{max} (neat) 2986, 2947, 2842, 1667, 1569, 1452, 1432, 1251, 1203, 1170, 1107, 1010, 949, 756, 694, 616 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{14}Br_4O_2N$ $[M + NH_4]^+$ 499.7717; found 499.7708.

Methyl 2,3,4-tribromo-5-methylbenzoate (8). Colorless solid **8**, yield 84%, R_f = 0.54 (15% EtOAc in hexane, silica gel tlc), mp 71–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H) 3.93 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.5, 139.6, 134.0, 131.5, 130.5, 129.9, 121.3, 52.9, 25.0; IR ν_{max} (neat) 2951, 2923, 2851, 1731, 1572, 1428, 1381, 1260, 1144, 1051, 989, 917, 891, 770, 641 cm^{-1}; HRMS (APCI) calcd for $C_9H_8Br_3O_2$ $[M + H]^+$ 386.8054; found 386.8052.

1,2,3,4-Tetrabromo-7,7-dimethoxy-5-(propan-2-ylidene)-bicyclo[2.2.1]hept-2-ene (10a). 10a,b, yield 98%, ratio of isomers 53 : 47, colorless liquid, R_f = 0.62 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.59 (s, 3H), 2.92 (d, 1H, J = 13.6 Hz), 2.41 (d, 1H, J = 13.6 Hz), 2.04 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.8, 129.5, 126.0, 125.3, 111.1, 72.7, 67.5, 52.3, 51.7, 42.6, 23.8; IR ν_{max} (neat) 3080, 2980, 2946, 2841, 1641, 1568, 1451, 1373, 1263, 1180, 1111, 971, 893, 842, 722, 647, 571 cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{15}Br_4O_2$ $[M + H]^+$ 510.7764; found 510.7762.

1,2,3,4-Tetrabromo-7,7-dimethoxy-5-(prop-1-en-2yl)bicyclo-[2.2.1]hept-2-ene (10b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.73 (s, 1H), 3.64 (s, 3H), 3.63 (s, 3H), 3.28 (dd, 1H, J = 9.3, 4.5 Hz), 2.54 (dd, 1H, J = 12, 9.3 Hz), 1.99 (dd, 1H, J = 12, 4.5 Hz), 1.82 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.8, 126.5, 125.5, 116.5, 112.3, 73.5, 68.3, 53.2, 52.3, 43.8, 19.6; IR (neat) 2916, 1717, 1607, 1546, 1455, 1343, 1228, 1187, 1092, 833, 763, 693, 638, 601 cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{15}Br_4O_2$ $[M + H]^+$ 510.7764; found 510.7762.

2,3-Dibromo-5-methyl-1*H*-inden-1-one (11). Yellow solid **11**, yield 94%, R_f = 0.6 (5% EtOAc in hexane, silica gel tlc), mp 91–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, 1H, J = 7.3, Hz), 7.08 (d, 1H, J = 7.3, Hz), 7.00 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 186.2, 145.8, 142.2, 129.7, 126.6, 123.1, 122.7, 122.3, 22.1; IR ν_{max} (neat) 3080, 2980, 2946, 2841, 1641, 1568, 1451, 1373, 1263, 1180, 1111, 971, 893, 842, 722, 647, 571 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_7Br_2O$ $[M + H]^+$ 302.8843; found 302.8837.

3-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)pentan-3-ol (14b). Colorless liquid **14b**, yield 98%, R_f = 0.53 (10% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.6 (s, 3H), 3.54 (s, 3H), 2.76 (dd,1H, J = 9.3, 4.9 Hz), 2.34 (dd, 1H, J = 11.2, 9.3 Hz), 2.11 (dd, 1H, J = 11.2, 4.9 Hz), 1.94–1.87 (m, 1H), 1.74–1.69 (m, 1H), 1.40–1.28 (m, 2H), 1.07 (s, 1H), 0.9 (t, 3H, J = 7.3), 0.81 (t, 3H, J = 7.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.6, 128.3, 112.3, 77.9, 75.7, 74.0, 52.8, 51.6, 51.0, 38.0, 29.2, 8.7, 7.1; IR ν_{max} (neat) 3605, 3493, 2970, 2883, 2845, 1607, 1457, 1278, 1193, 1117 cm^{-1}; HRMS (APCI) m/z calcd for $C_{14}H_{19}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 361.0062; found 361.0096.

4-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)heptan-4-ol (14c). Colorless solid **14c**, yield 99%, R_f = 0.5 (10% EtOAc in hexane, silica gel tlc), mp 66–68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 3H), 3.53 (s, 3H), 2.74 (dd, 1H, J = 9.3, 4.9 Hz), 2.34 (t, 1H, J = 10.0 Hz), 2.12 (dd, 1H, J = 11.2, 4.9 Hz), 1.88–1.81 (m, 1H), 1.59 (td, 1H J = 13.0, 4.4 Hz), 1.43–1.34 (m, 1H), 1.26–1.21 (m, 5H), 1.08 (s, 1H), 0.93–0.88 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 129.0, 128.3, 112.3, 77.9, 75.2, 73.9, 52.7, 51.6, 40.0, 39.6, 38.0, 17.8, 15.8, 14.4, 14.2; IR ν_{max} (neat) 3563, 2960, 2871, 1609, 1259, 1189, 1089, 1012, 794 cm^{-1}; HRMS (APCI) m/z calcd for $C_{16}H_{23}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 389.0423; found 389.0412.

1-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)cyclopentanol (14d). Colorless liquid **14d**, yield 91%, R_f = 0.5 (10% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.55 (s, 3H), 2.69 (dd, 1H, J = 9.3, 4.9 Hz), 2.44 (dd, 1H, J = 11.2, 9.3 Hz), 2.05 (dd, 1H, J = 11.7, 4.9 Hz), 1.88–1.80 (m, 3H), 1.79–1.70 (m, 2H), 1.65–1.57 (m, 2H), 1.46–1.40 (m, 1H), 1.08 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.9, 128.3, 112.5, 82.1, 78.2, 74.2, 55.0, 53.0, 51.6, 39.8, 39.6, 38.5, 23.8, 22.0; IR (neat) 3600, 2951, 2874, 2846, 1607, 1445, 1275, 1189, 1119, 1040, 985, 897, 798, 781 cm^{-1}; HRMS (APCI) m/z calcd for $C_{14}H_{17}Cl_4O_2$ $[(M + H)(-H_2O)]^+$ 358.9953; found 358.9945.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)butan-2-ol (15a). Colorless liquid **15a**, yield 99%, R_f = 0.56 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.55 (s, 3H), 2.67 (dd,1H, J = 9.3, 4.9 Hz), 2.36 (dd, 1H, J = 11.2, 9.3 Hz), 2.1 (dd, 1H, J = 11.2, 4.9 Hz), 1.42–1.36 (m, 5H), 1.14 (s, 1H), 0.88 (t, 3H, J = 7.6 Hz);

^{13}C NMR (400 MHz, $CDCl_3$) δ 128.9, 128.2, 112.4, 78.0, 74.1, 73.3, 53.3, 52.8, 51.6, 37.9, 34.8, 25.5, 7.8; IR ν_{max} (neat) 3603, 2950, 2847, 1606, 1458, 1381, 1275, 1186, 1114, 1035, 986, 905, 796, 724, 610 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{13}H_{19}Cl_4O_3$ $[M + H]^+$ 365.0059; found 365.0046.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)pentan-2-ol (15b). Colorless liquid **15b**, yield 98%, R_f = 0.51 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.54 (s, 3H), 2.67 (dd, 1H, *J* = 9.3, 4.9 Hz), 2.37 (dd, 1H, *J* = 11.2, 9.3 Hz), 2.11 (dd, 1H, *J* = 11.7, 4.9 Hz), 1.41 (s, 3H), 1.36–1.15 (m, 4H), 1.15 (br, 1H), 0.9 (br, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.8, 128.2, 112.4, 78.0, 74.1, 73.2, 53.6, 52.8, 51.6, 45.0, 37.9, 26.1, 16.7, 14.5; IR ν_{max} (neat) 3602, 2955, 2846, 1606, 1459, 1380, 1329, 1275, 1187, 1115, 1033, 905, 873, 802, 745, 616, 581 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{19}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 361.0109; found 361.0106.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)hexan-2-ol (15c). Colorless liquid **15c**, yield 94%, R_f = 0.51 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.54 (s, 3H), 2.67 (dd,1H, *J* = 9.3, 4.9 Hz), 2.39–2.33 (m, 1H), 2.11 (dd, 1H, *J* = 11.7, 4.9 Hz), 1.41 (s, 3H), 1.34–1.26 (m, 6H), 1.15 (br, 1H), 0.9 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.8, 128.2, 112.4, 77.9, 74.1, 73.2, 53.6, 52.8, 51.6, 42.2, 38.0, 26.2, 25.7, 23.1, 14.0; IR ν_{max} (neat) 3602, 2949, 2856, 1608, 1451, 1379, 1271, 1180, 1113, 1032, 985, 884, 801, 731, 615 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{26}Cl_4NO_3$ $[M + NH_4]^+$ 410.0637; found 410.0635.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)heptan-2-ol (15d). Colorless liquid **15d**, yield 96%, R_f = 0.53 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.55 (s, 3H), 2.67 (dd, 1H, *J* = 9.3, 4.9 Hz), 2.36 (dd, 1H, *J* = 11.2, 9.3 Hz), 2.11 (dd, 1H, *J* = 11.2, 4.9 Hz), 1.41 (s, 3H), 1.41–1.14 (m, 8H), 1.14 (br, 1H) 0.89 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.9, 128.2, 112.4, 78.0, 74.1, 73.2, 53.6, 52.8, 51.6, 42.5, 37.9, 32.2, 26.2, 23.2, 22.5, 14.0; IR ν_{max} (neat) 3604, 2947, 2855, 1606, 1459, 1380, 1275, 1190, 1115, 1034, 989, 889, 802, 736, 616 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{23}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 389.0422; found 389.0413.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)octan-2-ol (15e). Colorless liquid **15e**, yield 97%, R_f = 0.54 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.55 (s, 3H), 2.67 (dd, 1H, *J* = 9.3, 4.9 Hz), 2.36 (dd, 1H, *J* = 11.2, 9.3 Hz), 2.11 (dd, 1H, *J* = 11.2, 4.9 Hz), 1.41 (s, 3H), 1.33–1.26 (m, 10H), 1.15 (br, 1H) 0.88 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.8, 128.2, 112.4, 78.0, 74.1, 73.2, 53.6, 52.8, 51.6, 42.5, 37.9, 31.7, 29.7, 26.9, 23.5, 22.6, 14.0; IR ν_{max} (neat) 3606, 2932, 2853, 1606, 1459, 1379, 1332, 1275, 1191, 1114, 1034, 987, 905, 868, 804, 731, 616, 583 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{25}Cl_4O_2$, $[(M + H)^+(-H_2O)]^+$ 403.0579; found 403.0575.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)decan-2-ol (15f). Colorless liquid **15f**, yield 99%, R_f = 0.56 (5% EtOAc in hexane, silica gel tlc); 1H NMR (400 MHz, CDCl3) δ 3.58 (s, 3H), 3.53 (s, 3H), 2.65 (dd, 1H, *J* = 9.3, 4.9 Hz), 2.32 (dd, 1H, *J* = 11.2, 9.3 Hz), 2.09 (dd, 1H, *J* = 11.2, 4.9 Hz), 1.39 (s, 3H), 1.32–1.25 (m, 14H), 1.18 (br, 1H), 0.86 (t, 3H, *J* = 6.8 Hz); 13C NMR (400 MHz, CDCl3) δ 128.7, 128.2, 112.4, 77.9, 74.0, 73.1, 53.5, 52.7, 51.5, 42.5, 37.9, 31.8, 30.0, 29.4, 29.2, 26.1, 23.5, 22.5, 14.0; IR ν_{max} (neat) 3606, 2926, 2853, 1714, 1606, 1459, 1379, 1275, 1190, 1115, 1304, 989, 879, 804, 744, 616 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{29}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 431.0892; found 431.0898.

2-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)tetradecan-2-ol (15g). Colorless liquid **15g**, yield 98%, R_f = 0.58 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H), 3.53 (s, 3H), 2.66 (dd, 1H, *J* = 9, 4.6 Hz), 2.35 (dd, 1H, *J* = 11.2, 9.3 Hz), 2.1 (dd, 1H, *J* = 11.5, 4.6 Hz), 1.39 (s, 3H), 1.39–1.25 (m, 22H), 1.18 (br, 1H) 0.87 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 128.8, 128.2, 112.4, 77.9, 74.1, 73.1, 53.6, 52.7, 51.6, 42.5, 37.9, 31.9, 30.0, 29.6, 29.6, 29.5, 29.5, 29.3, 26.1, 23.5, 22.6, 14.1; IR ν_{max} (neat) 3608, 2852, 1606, 1460, 1379, 1275, 1191, 1115, 1035, 989, 873, 804, 723, 617 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{37}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 487.1518; found 487.1517.

1-Phenyl-2-(1,4,5,6-tetrachloro-7,7-dimethoxybicyclo[2.2.1]-hept-5-en-2-yl)propan-2-ol (15h). White solid **15h**, yield 98%, R_f = 0.52 (10% EtOAc in hexane, silica gel tlc), mp 98–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.14 (m, 5H), 3.58 (s, 3H), 3.54 (s, 3H), 2.73–2.67 (m, 2H), 2.56–2.45 (m, 2H), 2.33 (dd, 1H, *J* = 11.2, 4.9 Hz), 1.31 (s, 3H), 1.13 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 135.9, 130.8, 128.7, 128.4, 128.2, 126.8, 112.5, 78.0, 74.1, 72.9, 54.1, 52.8, 51.6, 48.1, 38.3, 26.1; IR ν_{max} (neat) 3585, 2979, 2949, 2844, 1605, 1494, 1453, 1381, 1279, 1190, 1116, 1096, 1032, 987, 910, 754, 727, 701, 607 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{19}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 409.0109; found 409.0110.

1-Phenyl-1-(1,4,5,6-tetrachloro-7,7-dimethoxybicyclo[2.2.1]-hept-5-en-2-yl)ethanol (15i). White solid **15i**, yield 99%, R_f = 0.61 (10% EtOAc in hexane, silica gel tlc), mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.30 (m, 2H), 7.24–7.22 (2H, m), 7.16–7.13 (1H, m), 3.49 (s, 3H), 3.46 (s, 3H), 2.97–2.94 (m,1H), 1.81–1.79 (m, 2H), 1.72 (s, 3H), 1.5 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 147.4, 128.9, 128.2, 126.8, 124.5, 112.4, 78.0, 74.5, 74.0, 55.4, 52.7, 51.6, 37.9, 30.4; IR (neat) ν_{max} 3585, 2954, 2924, 2848, 1603, 1442, 1326, 1261, 1180, 1160, 1098, 1066, 1029, 981, 900, 868, 782, 696, 581 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{17}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 394.9953; found 394.9949.

1-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)-1-*p*-tolylethanol (15j). White solid **15j**, yield 98%, R_f = 0.53 (5% EtOAc in hexane, silica gel tlc), mp 107–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, 2H, *J* = 8.3 Hz), 7.15 (d, 2H, *J* = 8.3 Hz), 3.58 (s, 3H), 3.56 (s, 3H), 3.03 (t, 1H, *J* = 7.3 Hz), 2.34 (s, 3H), 1.9 (d, 2H, *J* = 7.3 Hz), 1.79 (s, 3H), 1.53 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 144.6, 136.4, 128.9, 128.2, 124.5, 124.4, 78.0, 74.5, 74.0, 55.4, 52.8, 51.6, 38.0, 30.5, 20.9; IR ν_{max} (neat) 3548, 2984, 2945, 2847, 1606, 1507, 1447, 1359, 1280, 1194, 1109, 1079, 1033, 987, 904, 874, 814, 762, 721, 584 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{19}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 409.0109; found 409.0108.

1-(3-Methoxyphenyl)-1-(1,4,5,6-tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)ethanol (15k). White solid **15k**, yield

92%, R_f = 0.45 (5% EtOAc in hexane, silica gel tlc), mp 119–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, 1H, J = 8.1 Hz), 6.96–6.93 (m, 2H), 6.76 (d, 1H, J = 7.8 Hz), 3.80 (s, 3H), 3.57 (s, 3H), 3.54 (s, 3H), 3.04–3.01 (m, 1H), 1.90–1.88 (m, 1H), 1.78 (s, 3H), 1.56 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 159.6, 149.4, 129.3, 128.9, 128.3, 117.0, 112.4, 111.6, 111.0, 78.1, 27.5, 74.0, 55.2, 52.8, 51.6, 38.0, 30.4; IR ν_{max} (neat) 3483, 2948, 2844, 1605, 1581, 1484, 1435, 1317, 1280, 1182, 1152, 1035, 990, 913, 879, 789, 757, 706, 621 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{19}Cl_4O_3$ $[(M + H)^+(-H_2O)]^+$ 425.0058; found 425.0056.

1-(1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-yl)-1-*m*-tolylethanol (15l). White solid **15l**, yield 99%, R_f = 0.49 (5% EtOAc in hexane, silica gel tlc), mp 79–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (quin, 3H, J = 7.7 Hz), 3.60 (s, 3H), 3.56 (s, 3H), 3.04 (t, 1H, J = 7.1 Hz), 2.37 (s, 3H), 1.91 (d, 2H, J = 7.3 Hz), 1.80 (s, 3H), 1.55 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 147.5, 137.9, 128.9, 128.2, 128.1, 127.5, 125.2, 121.6, 112.4, 78.1, 74.5, 74.0, 55.4, 52.8, 51.7, 37.9, 30.5, 21.6; IR ν_{max} (neat) 3574, 2988, 2949, 2846, 1604, 1448, 1379, 1267, 1184, 1115, 1028, 984, 908, 880, 823, 786, 707, 616, 570, 616 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{19}Cl_4O_2$ $[(M + H)^+(-H_2O)]^+$ 409.0109; found 409.0105.

2,3-Dichloro-5-methyl-1*H*-inden-1-one (16a). Yellow solid **16a**, yield 83%, R_f = 0.44 (hexane, silica gel tlc), mp 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.25 (d, 1H, J = 7.3, Hz), 7.15 (d, 1H, J = 7.8, Hz), 2.44 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 192.1, 149.5, 148.8, 132.5, 132.0, 127.6, 123.8, 78.4, 73.0, 22.4; IR ν_{max} (neat) 2949, 2846, 1720, 1599, 1565, 1374, 1192, 1113, 829, 764, 697 cm^{-1}; HRMS (APCI) m/z calcd for $C_{10}H_7Cl_2O$ $[M + H]^+$ 212.9874; found 212.9862.

2,3-Dichloro-5-ethyl-4-methyl-1*H*-inden-1-one (16b). Yellow solid **16b**, yield 79%, R_f = 0.46 (hexane, silica gel, tlc), mp 75–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, 1H), 7.07 (d, 1H), 2.65 (q, 2H, J = 7.5, Hz), 2.54 (s, 3H), 1.2 (t, 3H, J = 7.3, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.9, 152.1, 151.7, 136.0, 131.8, 129.1, 128.1, 127.4, 121.0, 27.0, 14.3, 13.6; IR ν_{max} (neat) 2968, 2879, 1722, 1593, 1452, 1213, 1132, 846, 798, 718 cm^{-1}; HRMS (APCI) m/z calcd for $C_{12}H_{11}Cl_2O$ $[M + H]^+$ 241.0187; found 241.0176.

2,3-Dichloro-4-ethyl-5propyl-1*H*-inden-1-one (16c). Yellow solid **16c**, yield 75%, R_f = 0.41 (hexane, silica gel tlc), mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.25 (m, 1H), 7.3 (d, 1H J = 7.3, Hz), 3.01 (q, 2H, J = 7.3, Hz), 2.62–2.58 (m, 2H), 1.62 (sxt, 2H, J = 7.5, Hz), 1.23 (t,3H, J = 7.6, Hz), 1.01 (t, 3H, J = 7.3, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.7, 149.7, 138.3, 135.5, 130.4, 128.2, 127.6, 120.9, 34.9, 24.2, 20.0, 16.2, 14.1; IR ν_{max} (neat) 2961, 2872, 1722, 1593, 1555, 1450, 1203, 1131, 798, 741 cm^{-1}; HRMS (APCI) m/z calcd for $C_{14}H_{15}Cl_2O$ $[M + H]^+$ 269.0500; found 269.0496.

1,2-Dichloro-7,8-dihydroas-indacen-3(6*H*)-one(16d). Yellow solid **16d**, yield 71%, R_f = 0.45 (hexane, silica gel tlc), mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3 (d, 1H J = 6.8, Hz), 7.12 (d, 1H J = 7.3, Hz), 3.15 (t, 2H, J = 7.3 × 2, Hz), 2.88 (t, 2H, J = 7.3 × 2, Hz), 2.18–2.10 (2H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 186.1, 154.4, 150.8, 138.6, 134.6, 127.2, 127.0, 124.8, 121.8, 32.5, 30.2, 25.3; IR ν_{max} (neat) 2964, 2987, 2897, 1276, 1587, 1553, 1453, 1413, 1344, 1290, 1203, 1176, 1112, 787, 780 cm^{-1}; HRMS (APCI) m/z calcd for $C_{12}H_9Cl_2O$ $[M + H]^+$ 239.0030; found 239.0022.

2,3-Dichloro-4,5-methyl-1*H*-inden-1-one (17a). Yellow solid **17a**, yield 80%, R_f = 0.42 (hexane, silica gel tlc), mp 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, 1H, J = 7.3, Hz), 7.04 (d, 1H, J = 7.3, Hz), 2.48 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.7, 151.9, 146.1, 135.6, 132.4, 130.5, 127.4, 120.7, 21.0, 14.0; IR ν_{max} (neat) 2948, 2836, 1712, 1587, 1547, 1446, 1379, 1338, 1256, 1211, 1128, 965, 921, 848, 791, 760, 712 cm^{-1}; HRMS (ESI) m/z calcd for $C_{11}H_9Cl_2O$ $[M + H]^+$ 227.0030; found 227.0026.

2,3-Dichloro-4-ethyl-5-1*H*-inden-1-one (17b). Yellow solid **17b**, yield 80%, R_f = 0.49 (hexane, silica gel tlc), mp 56–58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, J = 7.3, Hz), 7.06 (d, 1H, J = 6.8, Hz), 3.00 (q, 2H, J = 7.7, Hz), 2.34 (s, 3H), 1.2 (t, 3H, J = 7.6, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.6, 145.3, 138.6, 135.2, 131.1, 128.2, 127.7, 120.9, 20.6, 20.0, 15.0; IR ν_{max} (neat) 2966, 2930, 2872, 1715, 1585, 1549, 1448, 1340, 1244, 1207, 1125, 1053, 973, 906, 860, 828, 770, 727 cm^{-1}; HRMS (ESI) m/z calcd for $C_{12}H_{11}Cl_2O$ $[M + H]^+$ 241.0187; found 241.0182.

2,3-Dichloro-5-methyl-4-propyl-1*H*-inden-1-one (17c). Yellow solid **17c**, yield 81%, R_f = 0.46 (hexane, silica gel tlc), mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, 1H, J = 7.3, Hz), 7.05 (d, 1H, J = 7.3, Hz), 2.92–2.88 (m, 2H), 2.32 (s, 3H), 1.60–1.51 (m, 2H), 1.04 (t, 3H, J = 7.1, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.7, 151.6, 145.5, 137.3, 135.4, 131.0, 128.2, 120.9, 29.3, 24.4, 20.2, 14.0 ν_{max}.33; IR (neat) 2960, 2929, 2871, 1720, 1588, 1553, 1456, 1346, 1232, 1212, 1131, 948, 844, 806, 772, 735 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{13}Cl_2O$ $[M + H]^+$ 255.0343; found 255.0328.

4-Butyl-2,3-dichloro-5-methyl-1*H*-inden-1-one (17d). Yellow solid **17d**, yield 79%, R_f = 0.43 (hexane, silica gel tlc), mp 49–51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, J = 7.3, Hz), 7.06 (d, 1H, J = 7.3, Hz), 2.96–2.92 (m, 2H), 2.33 (s, 3H), 1.55–1.42 (m, 4H), 0.98 (t, 3H, J = 7.6, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.7, 145.4, 137.5, 135.4, 131.0, 128.3, 127.7, 120.9, 33.2, 27.2, 23.1, 20.2, 13.9; IR ν_{max} (neat) 2957, 2925, 2863, 1720, 1588, 1552, 1457, 1343, 1219, 1129, 1030, 855, 806, 773, 731 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{15}Cl_2O$ $[M + H]^+$ 269.0500; found 269.0498.

2,3-Dichloro-5-methyl-4-pentyl-1*H*-inden-1-one (17e). Yellow solid, **17e** yield 88%, R_f = 0.43 (hexane, silica gel tlc), mp 79–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, J = 7.3, Hz), 7.06 (d, 1H, J = 7.3, Hz), 2.93–2.91 (m, 2H), 2.33 (s, 3H), 1.55–1.49 (m, 2H), 1.45–1.33 (m, 4H), 0.93 (t, 3H, J = 7.1, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.7, 145.4, 137.6, 135.4, 131.0, 128.3, 127.7, 120.9, 32.2, 30.8, 27.5, 22.4, 20.2, 14.0; IR ν_{max} (neat) 2955, 2927, 2858, 1723, 1585, 1554, 1461, 1345, 1223, 1132, 1081, 818, 804, 773, 735 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{17}Cl_2O$ $[M + H]^+$ 283.0656; found 283.0650.

2,3-Dichloro-4-heptyl-5-methyl-1*H*-inden-1-one (17f). Yellow solid, **17f** yield 77%, R_f = 0.49 (hexane, silica gel tlc), mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, J = 7.3, Hz), 7.06 (d, 1H, J = 7.3, Hz), 2.95–2.91 (m, 2H), 2.33 (s, 3H),

1.56–1.49 (m, 2H), 1.47–1.40 (m, 2H), 1.37–1.25 (m, 6H), 0.89 (t, 3H, J = 6.8, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.7, 145.4, 137.6, 135.4, 131.0, 128.3, 127.7, 120.9, 31.8, 31.2, 29.0, 27.5, 22.6, 20.2, 14.1; IR ν_{max} (neat) 2923, 2854, 1724, 1587, 1555, 1459, 1374, 1227, 1129, 1086, 977, 812, 767, 728 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{21}Cl_2O$ $[M + H]^+$ 311.0969; found 311.0963.

2,3-Dichloro-5-methyl-4-undecyl-1*H*-inden-1-one (17g). Yellow solid **17g**, yield 80%, R_f = 0.52 (hexane, silica gel tlc), mp 63–65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, 1H, J = 6.8, Hz), 7.05 (d, 1H, J = 7.3, Hz), 2.94–2.90 (m, 2H), 2.33 (s, 3H), 1.56–1.48 (m, 2H), 1.47–1.40 (m, 2H), 1.35–1.27 (m, 16H), 0.88 (t, 3H, J = 6.8, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.6, 145.4, 137.6, 135.3, 131.0, 128.3, 127.7, 120.9, 31.9, 31.1, 30.0, 29.3, 27.5, 22.7, 20.2, 14.1; IR (neat) 2920, 2851, 1718, 1587, 1552, 1458, 1216, 1130, 850, 809, 771, 730 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{29}Cl_2O$ $[M + H]^+$ 367.1595; found 367.1595.

2,3-Dichloro-5-methyl-4-phenyl-1*H*-inden-1-one (17h). Yellow solid **17h**, yield 77%, R_f = 0.48 (hexane, silica gel tlc), mp 149–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 4H), 7.18 (dd, 3H, J = 6.4, Hz), 2.03 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.8, 151.6, 145.4, 136.9, 135.9, 130.4, 129.3, 128.4, 128.2, 128.0, 126.9, 122.0, 21.1; IR ν_{max} (neat) 3047, 2922, 2859, 1718, 1588, 1553, 1444, 1372, 1336, 1219, 1225, 1125, 1083, 892, 832, 765, 726, 696, 648 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{11}Cl_2O$ $[M + H]^+$ 289.0187; found 289.0181.

2,3-Dichloro-5-phenyl-1*H*-inden-1-one (17i). Yellow solid **17i**, yield 84%, R_f = 0.42 (hexane, silica gel tlc), mp 98–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2H, J = 6.8, Hz), 7.52–7.42 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.5, 149.7, 147.7, 140.9, 139.2, 129.0, 128.8, 128.1, 127.3, 127.0, 126.9, 123.4, 118.7; IR ν_{max} (neat) 3040, 2919, 2861, 1726, 1603, 1565, 1452, 1418, 1340, 1303, 1213, 1109, 1008, 959, 856, 842, 750, 690 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_9Cl_2O$ $[M + H]^+$ 275.0030; found 275.0034.

2,3-Dichloro-5-*p*-tolyl-1*H*-inden-1-one (17j). Yellow solid **17j**, yield 97%, R_f = 0.49 (hexane, silica gel tlc), mp 138–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.43 (m, 4H), 7.38 (s, 1H), 7.8 (d, 2H, J = 7.8, Hz), 2.39, (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.5, 149.6, 147.6, 140.9, 138.9, 136.9, 129.7, 127.7, 127.3, 126.6, 123.4, 118.5, 21.2; IR ν_{max} (neat) 3010, 2911, 2831, 1719, 1601, 1663, 1455, 1424, 1337, 1301, 1216, 1169, 1116, 856, 810, 765, 696, 648 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{11}Cl_2O$ $[M + H]^+$ 289.0187; found 289.0182.

2,3-Dichloro-5-*m*-tolyl-1*H*-inden-1-one (17k). Yellow solid **17k**, yield 94%, R_f = 0.48 (hexane, silica gel tlc), mp 111–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.48 (m, 2H), 7.42–7.35 (m, 4H), 7.25 (d, 2H, J = 6.8, Hz), 2.45, (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.6, 149.7, 147.9, 140.8, 139.2, 138.7, 129.5, 128.9, 128.1, 127.7, 127.3, 126.8, 124.2, 123.4, 118.8, 21.5; IR ν_{max} (neat) 3014, 2918, 2848, 1714, 1604, 1565, 1455, 1379, 1338, 1219, 1112, 1036, 994, 880, 846, 787, 763, 696, 641 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{11}Cl_2O$ $[M + H]^+$ 289.0187; found 289.0178.

2,3-Dichloro-5-(3-methoxyphenyl)-1*H*-inden-1-one (17l). Yellow solid **17l**, yield 91%, R_f = 0.48 (hexane, silica gel tlc), mp 138–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.48 (m, 2H), 7.41–7.37 (m, 2H), 7.17 (d, 1H, J = 7.3, Hz), 7.10 (s, 1H), 6.96 (dd, 1H, J = 8.1, 2.2 Hz), 3.88 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 185.5, 160.0, 149.7, 147.5, 140.9, 140.7, 130.1, 128.2, 127.3, 127.1, 123.3, 119.5, 118.8, 113.9, 112.9, 55.4; IR ν_{max} (neat) 3013, 2917, 2849, 1714, 1606, 1566, 1462, 1339, 1281, 1199, 1168, 1115, 1048, 1019, 962, 848, 804, 769, 692, 660, 612 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{11}Cl_2O_2$ $[M + H]^+$ 305.0136; found 305.0135.

1,2,3,4-Tetrachloro-7,7-dimethoxy-5-(propan-2-ylidene)-bicyclo[2.2.1]hept-2-ene (18a). 18a,b, yield 98%, ratio of isomers 19 : 81, colorless liquid, R_f = 0.69 (5% EtOAc in hexane, silica gel tlc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 3H), 3.57 (s, 3H), 3.41 (d, 1H J = 2.9 Hz), 2.37 (d, 1H J = 13.7 Hz), 1.98 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.7, 129.3, 129.0, 125.8, 111.2, 79.2, 73.6, 52.1, 42.2, 23.6, 19.0; IR ν_{max} (neat) 2982, 2950, 2844, 1644, 1603, 1454, 1271, 1190, 1156, 1117, 1040, 985, 902, 756, 591 cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{13}Cl_4O$ $[(M + H)^+(-H_2O)]^+$ 312.9720; found 312.9790.

1,2,3,4-Tetrachloro-7,7-dimethoxy-5-(prop-1-en-2yl)bicycle-[2.2.1]hept-2-ene (18b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.98 (s, 1H), 4.70 (s, 1H), 3.62 (s, 3H), 3.55 (s, 3H), 3.23 (dd, 1H, J = 9.3, 4.4 Hz), 2.50 (dd, 1H, J = 12.2, 9.3 Hz), 1.93 (dd, 1H, J = 11.7, 4.4 Hz), 1.80 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.7, 129.1, 115.6, 112.2, 79.4, 74.5, 52.6, 51.8, 51.6, 40.6, 23.5; IR (neat) 2982, 2950, 2844, 1644, 1603, 1454, 1271, 1190, 1156, 1117, 1040, 985, 902, 756, 591 cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{13}Cl_4O$ $[(M + H)^+(-H_2O)]^+$ 312.9720; found 312.9790.

2,2-Dihydroxy-5-methyl-1*H*-indene-1,3(2*H*)-dione (19). To a stirred solution of 50 mg **11** (0.234 mmol) in acetonitrile (3 mL) at 0 °C was added Ru-LDH (20 mol%) and $NaIO_4$ (125 mg, 0.586 mmol) in water (1 mL). The mixture was stirred for 5 h at 0 °C–rt; after the reaction was complete (tlc monitoring), the resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (15 mL). Concentration of the filtrate followed by silica gel column chromatography afford white solid **19**, yield 84% (38 mg, 0.197 mmol), R_f = 0.23 (50% EtOAc in hexane, silica gel tlc), mp 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, 1H J = 7.8, Hz), 7.62 (s, 1H), 7.42 (d, 1H, J = 7.8, Hz), 7.70 (br, 2H), 2.47 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.0, 173.0, 143.2, 132.1, 132.0, 129.9, 129.6, 127.5, 21.4; IR ν_{max} (neat) 3403, 2925, 2855, 1752, 1720, 1600, 1428, 1381, 1257, 1224, 1192, 1093, 981, 907, 730 cm^{-1}; HRMS (APCI) m/z calcd for $C_{10}H_9O_4$ $[M + H]^+$ 193.0501; found 193.0496.

4-Ethyl-1,3-dioxo-5-propyl-2,3-dihydro-1*H*-indene-2,2-diyldiacetate (20a). White solid **20a**, yield 75%, R_f = 0.54 (20% EtOAc in hexane, silica gel tlc), mp 71–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, 1H J = 7.8, Hz), 7.64 (d, 1H J = 7.8, Hz), 3.17 (q, 2H, J = 7.3, Hz), 2.77–2.73 (m, 2H), 2.13 (s, 6H), 1.67 (sxt, 2H, J = 7.5, Hz), 1.19 (t, 3H, J = 7.6, Hz), 1.04 (t, 3H, J = 7.3, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 191.2, 190.2, 167.8, 150.9, 143.2, 138.2, 137.1, 136.8, 121.0, 34.7, 24.4, 21.2, 20.1, 14.6, 14.2; IR ν_{max} (neat) 2960, 2924, 2853, 1749, 1723, 1583, 1460,

1371, 1259, 1217, 1059, 961, 799, 755 cm^{-1}; HRMS (APCI) *m*/*z* calcd for $C_{18}H_{24}NO_6$ $[M + NH_4]^+$ 350.1604; found 350.1599.

1,3-Dioxo-1,2,3,6,7,8-hexahydroas-indacene-2,2-diyldiacetate (20b). White solid **20b**, yield 72%, R_f = 0.52 (20% EtOAc in hexane, silica gel tlc), mp 158–160 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, 1H *J* = 7.3, Hz), 7.69 (d, 1H *J* = 7.8, Hz), 3.31 (t, 2H, *J* = 7.6, Hz), 3.04 (t, 2H, *J* = 7.6, Hz), 2.24 (quin, 2H, *J* = 7.6, Hz), 2.13 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 191.3, 190.1, 167.9, 155.5, 143.3, 138.0, 134.7, 131.8, 121.9, 32.9, 32.9, 31.1, 25.2, 20.2; IR ν_{max} (neat) 2924, 2853, 1749, 1747, 1585, 1464, 1431, 1370, 1219, 1062, 976 cm^{-1}; HRMS (APCI) *m*/*z* calcd for $C_{16}H_{14}NaO_6$ $[M + Na]^+$ 325.0688; found 325.0677.

4-Ethyl-5-methyl-1,3-dioxo-2,3-dihydro-1*H*-indene-2,2-diyl-diacetate (20c). White solid **20c**, yield 79%, R_f = 0.56 (20% EtOAc in hexane, silica gel tlc), mp 145–147 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, 1H *J* = 7.8, Hz), 7.62 (d, 1H *J* = 7.8, Hz), 3.17 (q, 2H, *J* = 7.5, Hz), 2.49 (s, 3H), 2.13 (s, 6H), 1.18 (t, 3H, *J* = 7.6, Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 191.3, 190.3, 167.9, 146.6, 143.6, 138.2, 137.8, 136.4, 120.9, 21.6, 20.1, 19.4, 13.5; IR ν_{max} (neat) 2965, 2935, 1747, 1723, 1583, 1472, 1370, 1215, 1192, 1058, 1014, 956, 801, 753, 666 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{16}O_6Na$ $[M + Na]^+$ 327.0844; found 327.0837.

1,3-Dioxo-5-phenyl-2,3-dihydro-1*H*-indene-2,2-diyldiacetate (20d). White solid **20d**, yield 74%, R_f = 0.51 (20% EtOAc in hexane, silica gel tlc), mp 145–147 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.11–8.03 (m, 2H), 7.67 (d, 2H, *J* = 8.3, Hz), 7.53–7.46 (m, 3H), 2.15 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 190.7, 190.2, 168.1, 149.6, 139.9, 138.7, 137.6, 135.1, 129.2, 127.5, 124.0, 121.6, 20.0; IR ν_{max} (neat) 3020, 2926, 1749, 1719, 1599, 1423, 1260, 1214, 1017, 1056, 1012, 948, 801, 752, 697, 667 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{14}O_6Na$ $[M + Na]^+$ 361.0688; found 361.30675.

1,3-Dioxo-5-*p*-tolyl-2,3-dihydro-1*H*-indene-2,2-diyldiacetate (20e). White solid **20e**, yield 78%, R_f = 0.54 (15% EtOAc in hexane, silica gel tlc), mp 150–152 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.09–8.07 (m, 1H), 8.03–8.01 (m, 1H), 7.56 (d, 1H, *J* = 8.3, Hz), 7.31 (d, 1H, *J* = 8.3, Hz), 2.42 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 190.9, 190.2, 168.2, 149.7, 140.0, 139.6, 137.6, 135.9, 134.9, 130.1, 127.5, 124.1, 121.3, 21.3, 20.1; IR ν_{max} (neat) 3027, 2924, 1750, 1727, 1601, 1432, 1370, 1305, 1216, 1161, 1161, 1061, 1015, 945, 911, 816, 754, 553 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{20}NO_6$ $[M + NH_4]^+$ 370.1290; found 370.1288.

5-(3-Methoxyphenyl)-1,3-dioxo-2,3-dihydro-1*H*-indene-2,2-diyldiacetate (20f). White solid **20f**, yield 77%, R_f = 0.51 (20% EtOAc in hexane, silica gel tlc), mp 163–165 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.10–8.07 (m, 1H), 8.03–8.04 (m, 1H), 7.44–7.40 (m, 1H), 7.26–7.23 (m, 1H), 7.17 (d, 1H, *J* = 2.4, Hz), 7.00 (dd, 1H, *J* = 8.1, 2.2 Hz), 3.88 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 190.7, 190.1, 168.1, 149.5, 139.8, 137.7, 135.1, 130.3, 124.0, 121.6, 119.9, 114.8, 133.0, 55.4, 20.0; IR ν_{max} (neat) 3027, 2940, 2838, 1751, 1723, 1601, 1474, 1371, 1218, 1156, 1063, 1026, 957, 915, 844, 782, 732, 687 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{16}NaO_7$ $[M + Na]^+$ 391.0793; found 391.0787.

1,3-Dioxo-5-*m*-tolyl-2,3-dihydro-1*H*-indene-2,2-diyl diacetate (20g). White solid **20g** yield 76%, R_f = 0.53 (20% EtOAc in hexane, silica gel tlc), mp 159–161 °C, ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.07–8.05 (m, 1H), 8.01–7.99 (m, 1H), 7.45–7.35(m, 3H), 7.24–7.23 (m, 2H), 2.42 (s, 3H), 2.13 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 190.8, 190.2, 168.1, 149.8, 139.8, 139.0, 138.6, 137.5, 135.0, 130.0, 129.1, 128.3, 124.6, 124.0, 121.5, 21.5, 20.0; IRν_{max} (neat) 3025, 2923, 2852, 1748, 1720, 1601, 1463, 1415, 1305, 1216, 1156, 1089, 1053, 883, 794, 757 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{20}NO_6$ $[M + NH_4]^+$ 370.1290; found 370.1289.

Acknowledgements

FAK gratefully acknowledges CSIR for financial support. KRB thanks UGC for the award of a fellowship.

Notes and references

1 (*a*) L. F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 131; (*b*) H. Pellissier, *Chem. Rev.*, 2013, **113**, 442; (*c*) Y. Liu and J.-P. Wan, *Org. Biomol. Chem.*, 2011, **9**, 6873; (*d*) P. J. Parsons, C. S. Penkett and A. J. Shell, *Chem. Rev.*, 1996, **96**, 195; (*e*) F. Geng, J. Liu and L. A. Paquette, *Org. Lett.*, 2002, **4**, 71; (*f*) L. A. Paquette, *Eur. J. Org. Chem.*, 1998, 1709; (*g*) W. Giersch and I. Farris, *Helv. Chim. Acta*, 2004, **87**, 1601; (*h*) A. Srikrishna, S. Venkateswarlu, S. Nagaraju and K. Krishuan, *Tetrahedron*, 1994, **50**, 8765; (*i*) M. Hiersemann, L. Abraham and A. Pollex, *Synlett*, 2003, 1088; (*j*) L. F. Tietze, G. Brasche and K. M. Gericke, *Domino Reactions in Organic Synthesis*, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Die Deutsche Bibliothek, 2006.

2 (*a*) P. Wessig and J. Teubner, *Synlett*, 2006, 1543; (*b*) D. C. Harrowven, N. A. Newman and C. A. Knight, *Tetrahedron Lett.*, 1998, **39**, 6757; (*c*) W. M. Clark, A. M. Tickner-Eldridge, G. K. Huang, L. N. Pridgen, M. A. Olsen, R. J. Mills, I. Lantos and N. H. Baine, *J. Am. Chem. Soc.*, 1998, **120**, 4550; (*d*) M. A. Ernst-Russell, C. L. L. Chai, J. H. Wardlaw and J. A. Elix, *J. Nat. Prod.*, 2000, **63**, 129.

3 (*a*) R. E. McDevitt, M. S. Malamas, E. S. Manas, R. J. Unwalla, Z. B. Xu, C. P. Miller and H. A. Harris, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 3137; (*b*) M. Anstead, S. R. Wilson and J. A. Katzenellenbogen, *J. Med. Chem.*, 1989, **32**, 2163.

4 (*a*) L. M. X. Lopes, M. Yoshida and O. R. Gottlieb, *Phytochemistry*, 1984, **23**, 2021; (*b*) D. C. Harrowven, N. A. Newman and C. A. Knight, *Tetrahedron Lett.*, 1998, **39**, 6757.

5 C. H. Park, X. Siomboing, S. Yous, B. Gressier, M. Luyckxand and P. Chavatte, *Eur. J. Med. Chem.*, 2002, **37**, 461.

6 O. A. Akrawi, A. Khan, M. Hussain, H. Mohammed, A. Villinger and P. Langer, *Tetrahedron Lett.*, 2013, **54**, 3037.

7 J. A. Palermo, M. F. Rodriguez Brasco, C. Spagnuolo and A. M. Seldes, *J. Org. Chem.*, 2000, **65**, 4482.
8 R. L. Frank, H. Eklund, J. W. Richter, C. R. Vanneman and A. N. Wennerberg, *J. Am. Chem. Soc.*, 1944, **66**, 1.
9 G. M. Anstead, R. J. Altenbach, R. W. Scott and J. A. Katzenellenbogen, *J. Med. Chem.*, 1988, **31**, 1316.
10 (*a*) G. Jammaer, H. Martens and G. J. Hoornaert, *J. Org. Chem.*, 1974, **32**, 2163; (*b*) A. Chatterjee and S. Banerjee, *Tetrahedron*, 1970, **26**, 2599.
11 H. O. House and J. K. Larson, *J. Org. Chem.*, 1968, **33**, 448.
12 (*a*) S. Basurto, S. Garcia, A. G. Neo, T. Torroba, C. F. Marcos, D. Miguel, J. Barbera, M. B. Ros and M. R. de la Fuente, *Chem. – Eur. J.*, 2005, **11**, 5362; (*b*) E. N. Alesso, D. G. Tombari, A. F. Ibañez, G. Y. Moltrasio Iglesias and J. M. Aguirre, *Can. J. Chem.*, 1991, **69**, 1166.
13 H. E. Zimmerman, *J. Am. Chem. Soc.*, 1956, **78**, 1168.
14 K. Buggle, U. N. Ghógáin and D. O'Sullivan, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2075.
15 E. F. Ulman and W. A. J. Henderson, *J. Am. Chem. Soc.*, 1966, **88**, 4942.
16 (*a*) J. F. Feeman and E. D. Amstutz, *J. Am. Chem. Soc.*, 1950, **72**, 1522; (*b*) M. B. Floyd and G. R. J. Allen, *J. Org. Chem.*, 1970, **35**, 2647; (*c*) G. Jammaer, H. Martens and G. Hoornaert, *Tetrahedron*, 1975, **31**, 2293; (*d*) H. Martens and G. Hoornaert, *Synth. Commun.*, 1972, **2**, 147.
17 C. Manning, M. R. McClory and J. J. McCullough, *J. Org. Chem.*, 1981, **46**, 919.
18 (*a*) Y. Harada, J. Nakanishi, H. Fujihara, M. Tobisu, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2007, **129**, 5766; (*b*) B. J. Li, H.-Y. Wang, Q.-L. Zhu and Z.-J. Shi, *Angew. Chem., Int. Ed.*, 2012, **51**, 3948; (*c*) T. Morimoto, K. Yamasaki, A. Hirano, K. Tsutsumi, N. Kagawa, K. Kakiuchi, Y. Harada, Y. Fukumoto, N. Chatani and T. Nishioka, *Org. Lett.*, 2009, **11**, 1777; (*d*) K. Gao and N. Yoshikai, *Chem. Commun.*, 2012, **48**, 4305; (*e*) Y. Kuninobu, T. Matsuki and K. Takai, *Org. Lett.*, 2010, **12**, 2948; (*f*) N. B. Alexey, R. Beatrice, M. Lieven, S. Ian, A. Patrick, C. Andrei and C. Janine, *Org. Biomol. Chem.*, 2014, **12**, 728; (*g*) H. Tsukamoto and Y. Kondo, *Org. Lett.*, 2007, **9**, 4227; (*h*) R. C. Larock and M. J. Doty, *J. Org. Chem.*, 1993, **58**, 4579.
19 (*a*) F. A. Khan and C. H. Sudheer, *Org. Lett.*, 2008, **10**, 3029; (*b*) F. A. Khan and B. Rout, *Tetrahedron Lett.*, 2006, **47**, 5251.
20 (*a*) F. A. Khan, J. Dash, D. Jain and B. P. Das, *J. Chem. Soc., Perkin Trans. 1*, 2001, 3132; (*b*) F. A. Khan and L. Soma, *Tetrahedron Lett.*, 2007, **48**, 85; (*c*) F. A. Khan and S. Choudhury, *Eur. J. Org. Chem.*, 2006, 672.
21 F. A. Khan, J. Dash, N. Sahu and Ch. Sudheer, *J. Org. Chem.*, 2002, **67**, 3783.
22 (*a*) R. P. Lutz, *Chem. Rev.*, 1984, **84**, 205; (*b*) L. A. Paquette, J. L. Romine, H.-S. Lin and J. Wright, *J. Am. Chem. Soc.*, 1990, **112**, 9284. And references cited therein.
23 (*a*) R. B. Woodward, *Tetrahedron*, 1959, **5**, 70; (*b*) P. Yates and P. Eaton, *Tetrahedron Lett.*, 1960, 5; (*c*) P. Yates and P. Eaton, *Tetrahedron*, 1961, **12**, 13; (*d*) R. Breslow and J. M. Hoffman Jr., *J. Am. Chem. Soc.*, 1972, **94**, 2111.
24 E. T. McBee, W. R. Diveley and J. E. Burch, *J. Am. Chem. Soc.*, 1955, **77**, 385.
25 (*a*) F. A. Khan and N. Sahu, *J. Catal.*, 2005, **231**, 438; (*b*) F. A. Khan, B. Prabhudas, J. Dash and N. Sahu, *J. Am. Chem. Soc.*, 2000, **122**, 9558.
26 (*a*) R. R. Hark, D. B. Hauze, O. Petrovskaia and M. M. Joullié, *Can. J. Chem.*, 2001, **79**, 1632; (*b*) R. J. Heffner and M. M. Joullié, *Synth. Commun.*, 1991, **21**, 2231; (*c*) D. J. McCaldin, *Chem. Rev.*, 1960, **60**, 39; (*d*) M. B. Rubin, *Chem. Rev.*, 1975, **75**, 177; (*e*) A. Schönberg and E. Singer, *Tetrahedron*, 1978, **34**, 1283; (*f*) M. M. Joullié, T. R. Thompson and N. H. Nemeroff, *Tetrahedron*, 1991, **47**, 8791; (*g*) M. B. Rubin and R. Gleiter, *Chem. Rev.*, 2000, **100**, 1121; (*h*) J. Almog, A. Hirshfeld and J. T. Klug, *Forensic. Sci.*, 1982, **27**, 912.
27 (*a*) K. Bowden and S. Rumpal, *J. Chem. Soc., Perkin Trans. 2*, 1997, 983; (*b*) R. R. Hark, D. B. Hauze, O. Petrovskaia, M. M. Joullié, R. Jaouhari and P. M. McComiskey, *Tetrahedron Lett.*, 1994, **35**, 7719.

