Steric and electronic effects on the Weiss reaction. Isolation of 1:1 adducts

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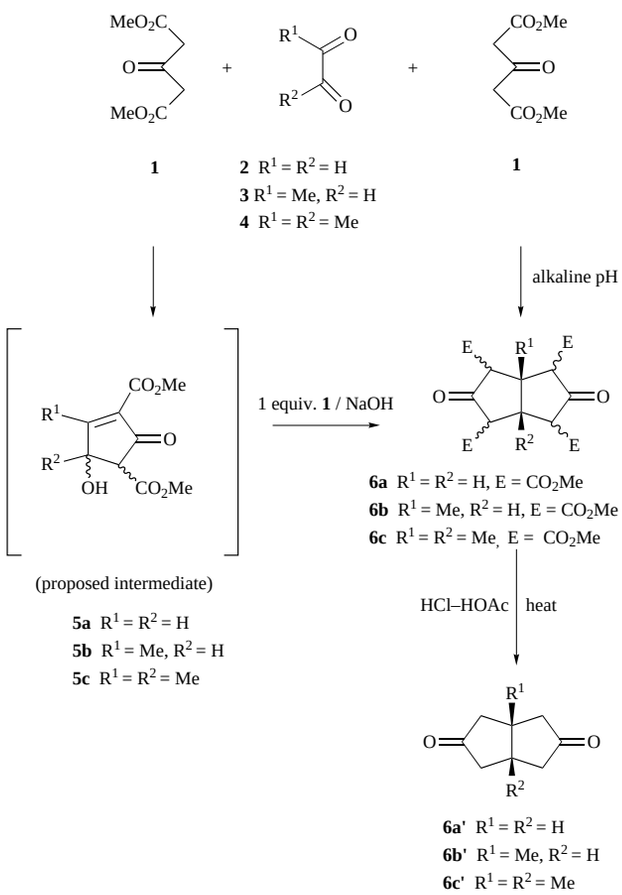
The mechanism of the Weiss reaction has been studied with respect to the intermediacy of 4-hydroxycyclopent-2-en-1-ones (1:1 adducts) in this process. Analysis of these experiments provides additional evidence that 4-hydroxycyclopentenones are indeed key intermediates in the Weiss reaction. Based on the reaction of dimethyl 3-oxoglutarate with benzil, pyridil, thenil, furil and phenanthrenequinone, steric effects play the major role in the overall success of this condensation to provide substituted *cis*-bicyclo[3.3.0]octane-3,7-diones. Moreover a trihydroxyindene [5.6] system (see 26) has been isolated for the first time under the Weiss conditions which provides additional support for the existence of cyclopentenone intermediates in this process.

Introduction

The majority of synthetic approaches to polyquinanes have been directed toward the preparation of specific natural products or of 'non-natural' compounds of computational importance. For a synthetic process or method to be termed general, it must provide a common route capable of extension to a variety of compounds of diverse structural type. The *cis*-bicyclo-[3.3.0]octane unit is the basic component of many polyquinane natural and non-natural products. At least one retrosynthetic pathway will always be present in this series of compounds which will terminate with the *cis*-bicyclo[3.3.0]octane system. The Weiss reaction has been shown to occur in a general fashion for a variety of 1,2-dicarbonyl compounds; 1,2-diketones, α-keto aldehydes, and glyoxal all react with dimethyl 3-oxoglutarate to yield the corresponding *cis*-bicyclo[3.3.0]octane tetraesters (Scheme 1). In this regard Bertz reported an approach to synthetic analysis[1] which employs graph and information theory in order to evaluate alternative synthetic routes toward a common target. Analysis of the Weiss reaction using this approach indicates that it ranks higher than the Diels–Alder reaction for the rapid generation of molecular complexity in a single step. Posner has referred to the Weiss process as a three component (2 + 3 + 3) coupling reaction and points out that an overall yield of 90% in this condensation can be viewed as an average yield of 97.5% for each of the new carbon–carbon bonds so formed.[2] The ability to produce a variety of monosubstituted and 1,5-disubstituted *cis*-bicyclo-[3.3.0]octane-3,7-diones by simply varying the substituents on the starting 1,2-dicarbonyl compound is a powerful feature of this process.

The versatility of the Weiss reaction has been demonstrated by the synthesis of many different cyclopentanoid systems including those of ellacene,[3] triquinacene,[4] modhephene[5] and gymnomitrol.[6] The mild conditions (room temp., pH 5.6–8.3) under which this condensation can be carried out should permit tolerance of a variety of functional groups (*e.g.* amides, halides, acetals, esters) to be manipulated later as desired. The interest in the reaction sequence **1** + **2** ⟶ **6** (Scheme 1) for the synthesis of polyquinane ring systems and natural products has, therefore, prompted a study of the influence of electronic and steric factors on the success of this condensation. The preparation of a number of 1,2-diones **2** in which the electronic and steric character of R^1 and R^2 have been varied is described below and is followed by an evaluation of their reactivity with **1**.

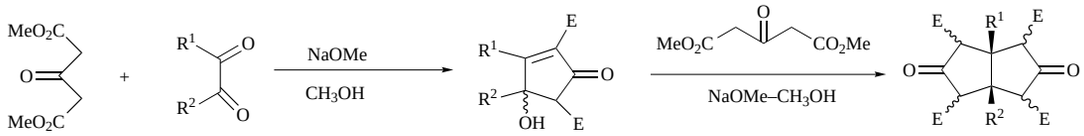


Scheme 1

1:1 Adducts

The mechanism of the Weiss reaction has been proposed[7] and can be subdivided into two principal processes; (i) the aldol sequence, and (ii) the Michael sequence. The aldol condensation of one molecule of glyoxal **2** with one molecule of dimethyl 3-oxoglutarate **1** is proposed to generate a β-hydroxy ketone which undergoes an intramolecular aldol reaction followed by dehydration to form the 4-hydroxycyclopenten-2-one **5** (a 1:1 adduct). The Michael reaction of enone **5** with another molecule of ketoglutarate **1**, which is followed by subsequent dehydration of the β-hydroxy ketone that results, produces an

Table 1

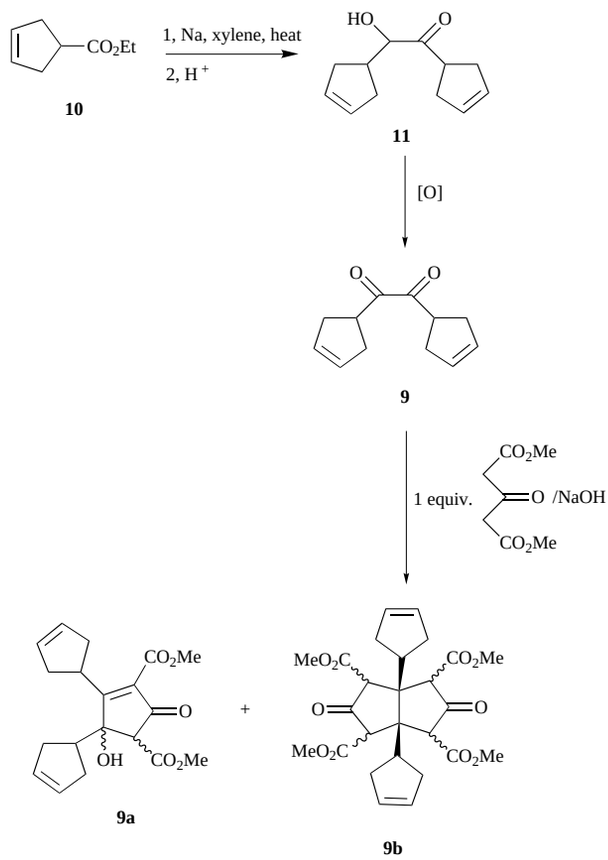


Dicarbonyl compound		R^1, R^2	1 : 1 Adduct (% yield)	1 : 2 Adduct (% yield)
1,2-Di(cyclopentyl)ethane-1,2-dione	**7**	cyclopentyl	**7a** (0)	**7b** (12–14)
1,2-Di(cyclohexyl)ethane-1,2-dione	**8**	cyclohexyl	**8a** (61)	**8b** (0)
1,2-Di(cyclopent-3-enyl)ethane-1,2-dione	**9**	cyclopent-3-enyl	**9a** (0)	**9b** (<10)
Benzil	**12**	Ph	**12a** (79)	**12b** (0)
Phenanthrenequinone	**13**	biphenyl-2,2′-diyl	**13a** (69)	**13b** (54)
1-Phenylpropane-1,2-dione	**14**	Ph, Me	**14a** (0)	**14b** (50–68)
Phenylglyoxal	**15**	Ph, H	**15a** (trace)	**15b** (>60)
2,2′-Pyridil	**16**	2-pyridyl	**16a** (67)	**16b** (0)
2,2′-Furil	**17**	2-furyl	**17a** (56)	**17b** (52)
2,2′-Thenil	**19**	2-thienyl	**19a** (77)	**19b** (0)

enone that is suitably set up for a second Michael addition. This reaction proceeds in an intramolecular fashion to provide the *cis*-bicyclo[3.3.0]octane-3,7-dione system **6** (1 : 2 adduct). In reactions with 1,2-dicarbonyl compounds such as glyoxal **2**, pyruvaldehyde **3** and butane-2,3-dione **4**, no 1 : 1 intermediates have been observed or trapped.[7] Consequently, the focus of the present study was directed toward the use of dicarbonyl compounds with suitable substituents (R^1 and R^2) to stabilize a 1 : 1 adduct which are capable of later addition of another molecule of dimethyl 3-oxoglutarate to provide the 1 : 2 adduct. This would furnish additional support for the involvement of a 4-hydroxycyclopenten-2-one intermediate in the Weiss reaction.

Steric interactions

Clearly the steric bulk of the substituent attached to the 1,2-dicarbonyl system plays an important role in the success of the Weiss reaction. Consequently, it was decided to investigate this process with 1,2-diones which are fully substituted with alicyclic groups. 1,2-Di(cyclopentyl)ethane-1,2-dione **7** and 1,2-di(cyclohexyl)ethane-1,2-dione **8** were synthesized and reacted (individually) with dimethyl 3-oxoglutarate **1** (Table 1). When the reactions were carried out under aqueous conditions (pH 5.6 or 8.3), only starting materials were recovered. When **7** was heated with dimethyl 3-oxoglutarate **1** in a solution of methanolic sodium hydroxide,[8,23] a 12–14% yield of the bicyclic 1 : 2 adduct **7b** was obtained. Under the same conditions, the di(cyclohexyl) analog **8** failed to produce any 1 : 2 adduct **8b**, however, when allowed to stir at room temp. for 9 days a 61% yield of the 1 : 1 adduct, 4-hydroxycyclopentenone **8a**, was observed. Apparently, the di(cyclohexyl)ethane-1,2-dione **8** reacted with one molecule of **1** to form the intermediate 1 : 1 adduct **8a**, which was too crowded sterically to allow addition of a second molecule of **1** to the enone system. The 1,2-di(cyclopent-3-enyl)ethane-1,2-dione **9** was prepared in two steps starting from ethyl cyclopent-3-enecarboxylate **10** by the method of Stocker (Scheme 2).[9] The oxidation of **11** with copper acetate[10] provided the desired diketone **9**, albeit in poor yield (27%). Rigby[11] had reported that bismuth trioxide served as a mild oxidant for acyloins in cases where copper reagents failed. When Bi_2O_3 was used for the oxidation of **11**, the yield of **9** was increased to 52%. When **9** was stirred with dimethyl 3-oxoglutarate, under a variety of conditions, the formation of a low yield of the bicyclic 1 : 2 adduct **9b** and a material with the spectral characteristics of the 1 : 1 adduct **9a** was observed. The CI mass spectrum of this material contained the molecular ion of **9b** at *m*/*z* 503 and an ion for **9a** at *m*/*z* 347. Repeated attempts at column chromatography provided a material enriched in **9a**, but this 1 : 1 adduct proved too unstable for isolation and complete characterization. Formation of **9b** was apparently retarded by steric interactions since all attempts to improve the yield of this 1 : 2 adduct were unsuccessful.



Scheme 2

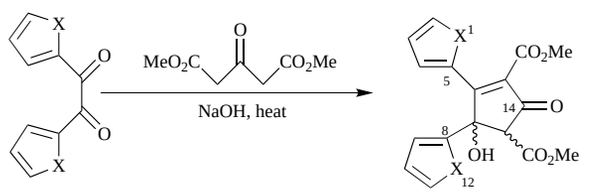
From these results, it appeared that substituents which occupy a 'molecular volume' smaller than a cyclopentane unit (as in **7**) would serve as useful substrates in this condensation, while those which contain the cyclohexyl rings would not react in the Weiss reaction to provide 1 : 2 adducts. The formation of both the 1 : 1 and 1 : 2 adducts from di(cyclopentenyl)ethane-1,2-dione provides additional support for the involvement of a 4-hydroxycyclopentenone intermediate in the mechanism of the Weiss reaction. Unfortunately, the instability of this 1 : 1 adduct **9a** did not permit investigation of this hypothesis.

Electronic effects

Earlier work had demonstrated that reaction of dimethyl 3-oxoglutarate with benzil **12** furnished a stable 4-hydroxycyclopentenone 1 : 1 adduct **12a**. The failure of benzil to provide a 1 : 2 adduct was felt to arise from electronic as well as steric factors since phenanthrenequinone, under analogous conditions, gave a similar result.[7] In phenanthrenequinone **13**, the

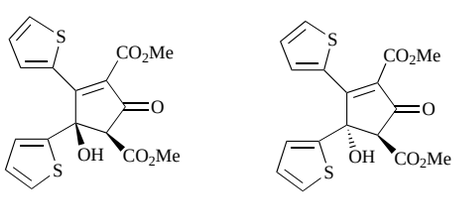
phenyl substituents of the 1,2-dicarbonyl system are constrained in a six-membered ring, consequently, steric factors in this case were considered minimal since the aromatic substituents are tied back in the ring system. These two experiments with benzil and phenanthrenequinone indicated that electronic factors (stabilization of the intermediate enone by the aromatic π system) may play a role in the lack of reactivity of **1** with these substrates; however, in the case of benzil, steric factors may also be involved. Phenylglyoxal **15**, on the other hand, gave a 1:2 adduct with **1** accompanied by a 1:1 adduct observed by spectroscopy but too unstable to isolate.[6] Furthermore, 1-phenylpropane-1,2-dione **14** reacted in a similar fashion with **1** to provide the 1:2 adduct **14b**. When **14** was stirred with **1** in either aqueous sodium hydrogen carbonate or in methanolic sodium methoxide the formation of the 1:2 adduct **14b** was observed in 68 and 50% yields, respectively.

Pyridil **16**, a heterocyclic analog of benzil, behaved in a similar fashion. When **16** was stirred with excess **1** in a methanolic solution of sodium methoxide a yellow precipitate (sodium salt) was formed. After the usual work-up (aqueous HCl) a 69% yield of the di(pyridyl) substituted 1:1 adduct **16a** was obtained (Scheme 3). No material which could be identified as the 1:2



16 X = -C=N-(pyridine)
17 X = O (furan)
19 X = S (thiophene)

16a X= -C=N-(pyridine)
17a X = O (furan)
19a X = S (thiophene)



20a **20b**

Scheme 3

adduct **16b** was isolated from this reaction or from the same reaction when repeated at a higher temperature (60 °C) in the presence of additional glutarate **1**. In order to determine the involvement of the 4-hydroxycyclopentenone intermediate in the Weiss reaction, it was necessary to find a 1,2-dicarbonyl compound which formed both isolable 1:1 and 1:2 adducts. Furthermore, for proof that the 1:1 adduct was indeed an intermediate it was necessary to demonstrate that addition of one equivalent of dimethyl 3-oxoglutarate to the monocyclic 1:1 adduct would result in the formation of the *cis*-bicyclo[3.3.0]octane-3,7-dione system. Consideration of both steric and electronic effects suggested that a 1,2-dicarbonyl compound which carried substituents with less steric bulk than phenyl or cyclohexyl groups and possessed the capability to stabilize the reactive π system of the 4-hydroxypentenone intermediate would be required. The 2,2′-furil **17** appeared to be an ideal candidate. It is substituted with two aromatic groups, the π-systems of which would stabilize the 1:1 adduct, and the furan rings of furil are smaller than benzene, pyridine and cyclohexane and might permit the addition of a second equivalent of dimethyl 3-oxoglutarate **1** to the 1:1 adduct.

When 2,2′-furil **17** was heated with **1** in a solution of NaOH and methanol, a precipitate formed. Examination of the ^{1}H NMR spectrum and mass spectrum of this material indicated that the 1:2 adduct **17b** had been obtained. Treatment of this sodium salt with aqueous HCl provided the di(furyl) substituted *cis*-bicyclo[3.3.0]octane-3,7-dione tetraester **17b** in 52% yield from **17**.[12] When 2,2′-furil and dimethyl 3-oxoglutarate were reacted in a 1:1 stoichiometry, under the same conditions, a new component was observed by TLC, accompanied by a considerable amount of baseline material. In order to avoid decomposition, the crude material was eluted rapidly under nitrogen through a short silica gel column providing **17a** in pure form as a light yellow solid (1:1 adduct) in 56% yield. The isolation and characterization of a stable 1:1 adduct **17a** accompanied by the *cis*-bicyclo[3.3.0]octane-3,7-dione tetraester **17b** from the same dicarbonyl compound provides strong evidence for the intermediacy of a 4-hydroxycyclopentenone on the reaction coordinate of the Weiss reaction.

The ability of **17a** to add a second molecule of dimethyl 3-oxoglutarate could be attributed to either differences in size or electronic character of the aromatic substituents on the 1,2-dicarbonyl compound. In order to better differentiate the effect of size or electronic character of the substituents on the Weiss reaction, it was decided to investigate the reaction of 2,2′-thenil with dimethyl 3-oxoglutarate. This would allow a comparison of the effect of thiophene rings on the condensation relative to that of benzene and furil. The 1,2-dione, 2,2′-thenil **19**, was prepared in two steps from commercially available thiophene-2-carbaldehyde.[13–15] The 1:1 adduct **19a** was prepared under the conditions analogous to those employed earlier for preparation of the furil analog **17a**. Sodium dimethyl 3-oxoglutarate was prepared in methanol and 2,2′-thenil was added at room temp. resulting in precipitation of the sodium salt of the 1:1 adduct. Treatment of this material with aqueous HCl provided the di(thienyl) substituted 1:1 adduct **19a** in 77% yield (Scheme 3). This material proved to be more stable than the furil 1:1 adduct and could be easily purified by gravity column chromatography. Both the CI and EI mass spectra of the 1:1 adduct **19a** contained fragment ions which were similar to those of **17a**, furthermore the ^{1}H and ^{13}C NMR spectra were consistent with the proposed structure of **19a**. The methoxy groups appeared as two singlets in the proton spectrum at δ 3.72 and 3.84, respectively. The signal which represented the hydroxy proton at δ 5.42 disappeared upon treatment with D_2O. The carbon spectrum contained 17 lines and the cyclopentanone carbonyl carbon atom appeared at δ_C 190.0, consistent with the signal from this group observed in related molecules. Examination of both the ^{1}H and ^{13}C NMR spectra of this solid indicated the presence of a second isomer (<10%). The 1:1 adduct **19a** could potentially exist in two epimeric forms, represented by **20a** and **20b**. The 2,2′-thenil **19** was then heated with 2 equiv. of dimethyl 3-oxoglutarate in the presence of NaOMe–MeOH to determine if a 1:2 adduct would result. Although the presence of **19a** was observed by TLC, heating the mixture for 16 h in refluxing methanol did not provide any indication of the presence of a 1:2 adduct **19b**. The IR, ^{1}H NMR and mass spectra of the reaction mixture were consistent with the presence of the 1:1 adduct **19a** and dimethyl 3-oxoglutarate. An attempt to add dimethyl 3-oxoglutarate to the 1:1 adduct **19a** directly was likewise unsuccessful.

Evaluation of steric and electronic influences on the success of the Weiss reaction

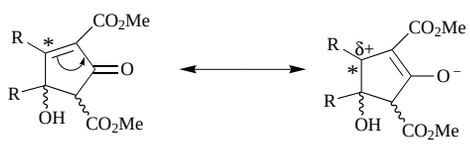
The failure of 2,2′-thenil to form a 1:2 adduct could result from either steric effects, electronic effects, or a combination of both. It was difficult to resolve whether these observations were due to steric congestion in the intermediate 1:1 adduct [as in the case of the di(cyclohexyl) analog **8**], or to electron release to the enone system decreasing the reactivity of the 1:1 adduct toward Michael addition of a second molecule of dimethyl 3-oxoglutarate. Previously it was felt that both electronic and steric effects were important in the success of the Weiss condensation, since dimethyl 3-oxoglutarate and phenanthrenequinone yielded only a 1:1 adduct upon reaction with excess dimethyl 3-oxoglutarate.[7] In the case of phenanthrenequinone,

Table 2

Substituent $R^1 = R^2$ 1 : 1 adduct	* δ_C of β carbon in 1 : 1 adduct	Aldehyde (control)	δ_C of carbonyl carbon
8a Cyclohexyl	186.5	cyclohexanecarbaldehyde	202.1 (ref. 24*a*)
		acetaldehyde	200.5 (ref. 24*a*)
12a Phenyl	175.0	benzaldehyde	190.7 (ref. 24*a*)
17a 2-Furyl	164.1	2-furaldehyde	178.2 (ref. 22)
19a 2-Thienyl	153.0	2-thienaldehyde	182.9 (ref. 24*b*)

the effect of steric congestion should be less important. This is due to the unique position of the aromatic substituents which are tied back in a ring which occupies a molecular volume similar to that in cyclohexane-1,2-dione at the site of reaction, as mentioned earlier.

The ability of furil to proceed to the 1 : 2 adduct in contrast to the results with thenil, benzil and pyridil was important. Although thiophene and furan are five-membered heterocycles, thiophene is larger than furan as a consequence of the size of the sulfur atom. The atomic radius of oxygen is reported to be 0.74 Å, and its van der Waals radius is 1.40 Å. In contrast, the atomic radius for sulfur is 1.04 Å and its van der Waals radius is 1.85 Å.[16] Examination of models of these substituents indicated that benzene and thiophene are similar in size, and are both larger than furan. The electronic nature of these substitutions also varies. The electronic effects deemed important here are those that would alter the electron density at the β-position of the enone system of the 1 : 1 adduct (Scheme 4). Substituents



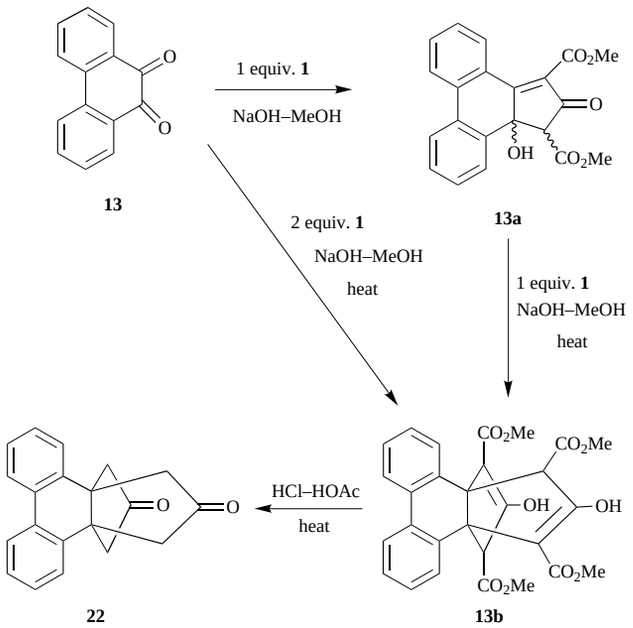
Scheme 4

capable of donating electrons to this site (designated as *) would be expected to render the enone system less electrophilic, thereby decreasing the rate of the Michael addition of dimethyl 3-oxoglutarate to the enone in favor of competing side reactions such as the formation of cyclopentadienones. A number of criteria can be used to judge the electronic nature of these aromatic groups. The resonance energy of these substituents can serve to gauge how well their π-electrons are delocalized, and therefore, their ability to donate electron density to the enone system of the 1 : 1 adducts. Resonance energies for these compounds follow the order: benzene > pyridine > thiophene > furan.[17–19] On the basis of resonance energies, the furan substituent should be better able to donate electron density to the enone system of the 1 : 1 adduct than either thiophene or benzene rendering this Michael acceptor the least electrophilic. The acid strength of the corresponding carboxylic acids follows the order: furan-2-carboxylic acid > thiophene-2-carboxylic acid > benzoic acid. This order of acidities indicates that the 2-furyl and 2-thienyl substituents are able to withdraw electrons through an inductive mechanism to a greater extent than benzene. Another measure of the electronic nature of these substituents is the experimental Hammett σ^+ values. These values have been employed to gauge electronic effects in cases where direct conjugation is possible and should be appropriate for the substituted 1 : 1 adducts. The σ^+ values for this series of compounds were reported by Hill *et al.* to be: phenyl (1.0), 2-thienyl (−0.85) and 2-furyl (−0.95).[20] These data suggested that the di(furyl) 1 : 1 adduct should be less reactive than either the benzil or thenil 1 : 1 adducts based entirely on electronic factors. *This is contrary to the observed results!*

To evaluate the effect of the substituent on the electron density of the β-carbon atom of the enone system in various 1 : 1 adducts, ^{13}C NMR spectroscopy was employed. The chemical shifts are listed in Table 2. While it is true that ^{13}C chemical shifts do not depend entirely on electron density, the correlation between the two is often good in a similar series of compounds.[21] For example, the decreased electron density at the β carbon of α,β-unsaturated ketones is responsible for the downfield shift of this signal (δ 165.2 for 2-cyclopentenone *vs.* δ 130.8 for cyclopentene) relative to that of cyclopentene.[22] The assignment of chemical shifts for the β-carbon of the 1 : 1 adducts could not be made simply on the basis of the broad-band (BB) decoupled ^{13}C NMR spectrum. Although this signal would be expected to occur around δ 160, the spectra of the 1 : 1 adducts contained many peaks in the region from δ 150–170. To determine the assignments, the quaternary carbons were first defined through the NORD (noise off-resonance decoupled) ^{13}C NMR spectrum. The ^1H-coupled, ^{13}C NMR spectrum was then recorded and examined. It was possible to make assignments for all the carbon atoms of the cyclopentenone system. The values for the chemical shifts of the β-carbons of the enone system in the 1 : 1 adducts were compared to those for the carbonyl carbons of the corresponding substituted aldehydes. In these aldehydes, it is anticipated that the chemical shift should be influenced by the electronic interaction of the substituent with the carbonyl function. A good correlation can be seen between the chemical shifts of the β-carbons of the 1 : 1 adducts and the corresponding shifts of the aldehydic carbonyl carbon atoms. In addition there is a reasonable correlation between the chemical shifts of these carbon atoms and their σ^+ values. These pieces of evidence, taken together, would tend to rank the electron density of the β-carbon atom of the enone system of the 1 : 1 adduct in the order of 2-furyl **17** > 2-thienyl **19** > phenyl **12** > cyclohexyl **8**. This order should be opposite to their ability to act as Michael acceptors, for the higher electron density on the β-carbon of the enone system would be expected to render this site less reactive toward Michael addition. On this basis, the 1 : 1 adduct of benzil should be better suited, electronically, to add a second molecule of dimethyl 3-oxoglutarate than the 1 : 1 adduct of furil. *This is again exactly opposite to the experimental observations!* This study suggests that the predominant effect in the conversion of the 1 : 1 adduct into the 1 : 2 adduct in the series of aromatic substituted 1,2-dicarbonyl compounds rests on steric factors, analogous to the results observed for **8**.

Reactions of phenanthrenequinone with dimethyl 3-oxoglutarate

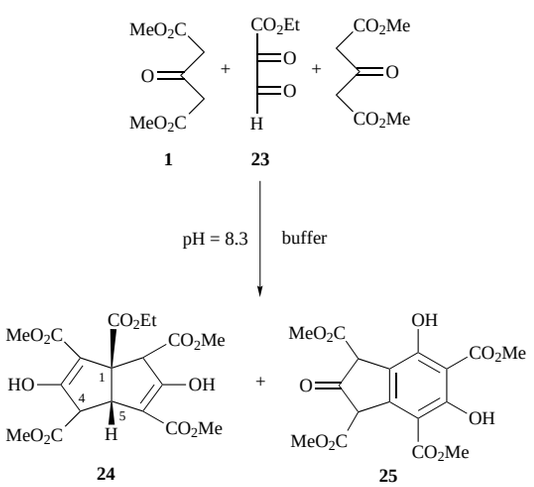
The above results prompted the reinvestigation of the reaction of phenanthrenequinone **13** with dimethyl 3-oxoglutarate. If electronic effects are less important in the formation of 1 : 2 adducts from aromatic substituted 1,2-diketones than steric effects, then phenanthrenequinone should be capable of adding two molecules of dimethyl 3-oxoglutarate to form the bicyclic 1 : 2 adduct **13b** (Scheme 5). When the reaction was repeated under the conditions reported earlier[25] (NaOH, MeOH) at room temperature, the sodium salt of **13a** was again found to precipitate from the reaction mixture. The earlier inability to convert **13a** into **13b**[7] appeared to result from problems of solubility, followed by decomposition of **13a**. To circumvent this difficulty, phenanthrenequinone was reacted with dimethyl 3-oxoglutarate at higher dilution and higher temperature (NaOH, MeOH, 68 °C) which resulted in the formation of a white solid. Examination of the ^1H and ^{13}C NMR spectra of the material indicated the presence of a single isomer with two-fold symmetry consistent with



Scheme 5

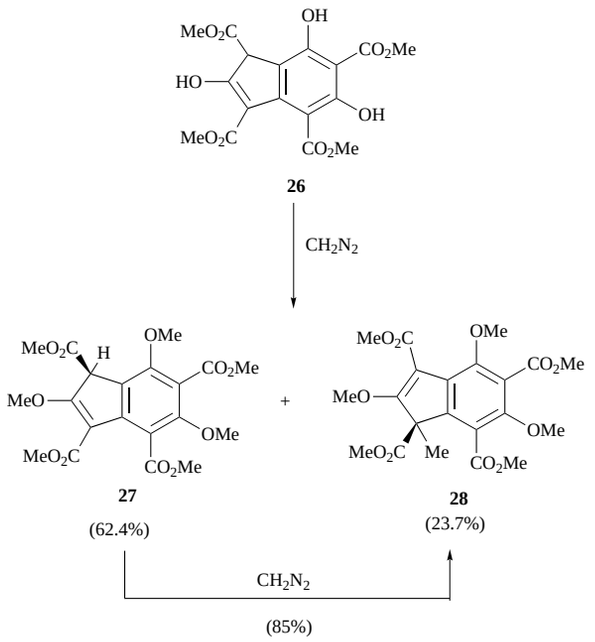
structure **13b**. Hydrolysis of **13b** and decarboxylation provided a 93% yield of the biphenylene fused *cis*-bicyclo[3.3.0]octane-3,7-dione system **22**. In addition, the bicyclic 1 : 2 adduct was also formed by adding dimethyl 3-oxoglutarate to the 1 : 1 adduct, heating 1 : 1 adduct **13a** and **1** in methanolic sodium hydroxide for 5 h resulted in the formation of **13b** in 53% yield. Dimethyl 3-oxoglutarate **1** was also added to **13a** at room temperature, although only in 29% yield. The formation of **13b** from **13a** serves as additional proof for a 4-hydroxycyclopentenone intermediate involved in the Weiss reaction.

Recently the reaction of **1** with ethyl 2,3-dioxopropionate **23** was examined under the Weiss reaction conditions and provided the first case of the formation of a [5.6] indene ring system **25**. As shown in Scheme 6, 2 equiv. of **1** and 1 equiv. of **23**



Scheme 6

were dissolved in $NaHCO_3$ buffer (pH = 8.3) and stirred at room temp. for 3 days to provide a mixture of **24** and **25**. The normal Weiss condensation product **24** and the trihydroxyindene [5.6] system **25** were obtained in 26 and 35% yields, respectively. The [5.6] system **25** was isolated as a mixture of isomers including some of the enol form **26**. This is the first report of the origin of a [5.6] indene system from the Weiss reaction and may lead to extension of this process to other [5.6] related systems. The structure of the trihydroxyindene [5.6] system **25** was confirmed on examination of the IR, NMR and MS data as well as X-ray analysis of the corresponding trimethoxy derivative **27**.[26] When indene **26** was treated with CH_2N_2 over a period of 6 h, both 2,5,7-trimethoxyindene **27** and 2,4,6-trimethoxy-1-methylindene **28** were obtained (Scheme 7). Furthermore when **27** was exposed overnight to CH_2N_2, the tetramethylated material **28** was isolated in 85% yield. Outlined in Scheme 8 is a proposed mechanism for the formation of dihydroxyindene **25** through an intermediate 1 : 1 adduct **29** and cyclopentenone **31**. It is believed 4-hydroxycyclopentenone **29** underwent a Michael addition with an additional equivalent of oxoglutarate **1** and this was followed by subsequent loss of water to furnish cyclopentenone **31** which can undergo cyclization by path **a** (Weiss path) or path **b**. Path **a** provides the 1 : 2 adduct **24** characteristically derived from the Weiss process; however, reaction by path **b** provides indene **25** presumably through keto tautomer **32**. Both products which were isolated and characterized provide additional support for the existence of cyclopentenones such as **29** and **31** in the Weiss reaction.



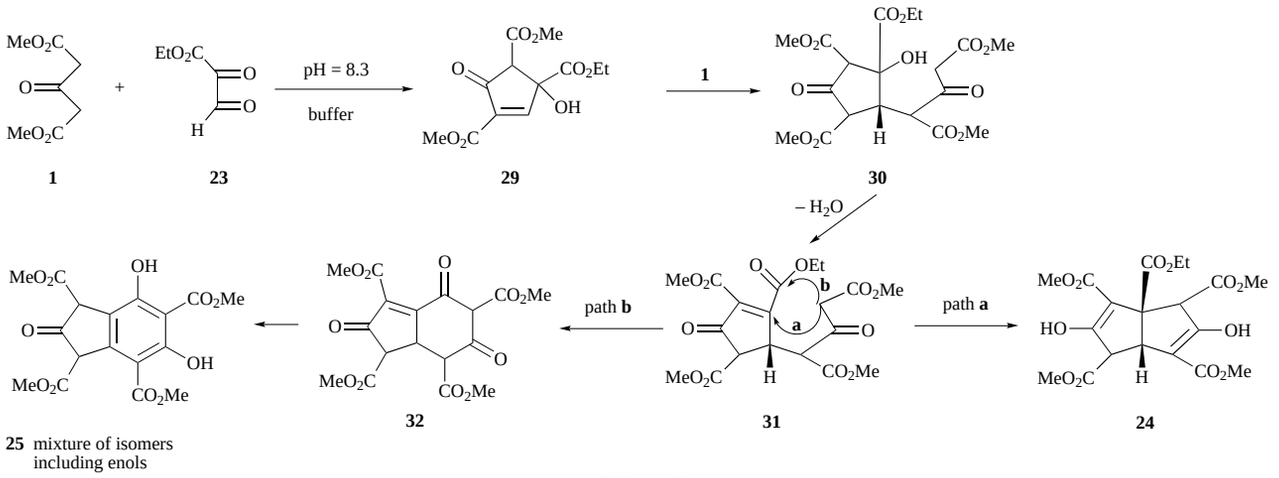
Scheme 7

Experimental

The experimental details are analogous to those reported earlier.[7,11] All materials were commercially available and used as received, except where indicated. Ether refers to diethyl ether. Petroleum refers to light petroleum boiling in the range 40–60 °C. Analytical TLC plates used were E. Merck Brinkman UV-active silica gel or alumina on plastic. Compounds were visualized by UV light, 2,4-DNP and $FeCl_3$ spray reagents or iodine vapor. The 2,4-DNP spray reagent was composed of 2,4-dinitrophenylhydrazine, ethanol and sulfuric acid. The ferric chloride spray reagent was prepared by dissolving ferric chloride (2.0 g) in 100 cm^3 of water. In the NMR spectral data *J* values are given in Hz.

1,2-Di(cyclopentyl)ethane-1,2 dione 7

To a 500 cm^3 round bottom flask equipped with a magnetic stirrer, heating mantle, Dean–Stark trap and reflux condenser, was added cyclopentanecarboxylic acid (32.1 g, 0.28 mol), dry benzene (250 cm^3), absolute ethanol (70 cm^3) and sulfuric acid (conc., 1 cm^3). The mixture was heated at reflux for 30 h. The excess ethanol and benzene were removed by distillation at atmospheric pressure. The crude product was washed with aqueous $NaHCO_3$ solution (10%, 100 cm^3) and brine (100 cm^3). The crude product was purified by distillation under reduced pressure to provide 29.5 g (74%) of ethyl cyclopentanecarboxylate, bp 80–85 °C (water aspirator); ν_{max}/cm^{-1} 2950, 1725 and 1150; δ_H(60 MHz; $CDCl_3$) 1.26 (3 H, t, *J* 7, CH_3CH_2), 1.43–2.20 (8 H, m),



Scheme 8

2.20–3.13 (1 H, m), 4.13 (2 H, q, *J* 7, CH_3CH_2); *m*/*z* (CI) 143 ($M^+ + 1$, 100). This material was used directly in the next step.

In a three-neck 500 cm^3 round bottom flask fitted with a reflux condenser, a fine dispersion of sodium metal was prepared (10.0 g, 0.43 mol). The sodium metal was washed by withdrawing the solvent through a sintered filter stick under vacuum followed by addition of fresh xylene (50 cm^3) and dry ether. Dry ether (200 cm^3) was added and the solution rapidly stirred. Ethyl cyclopentanecarboxylate (26.7 g, 0.20 mol) was dissolved in dry ether (50 cm^3) and added dropwise over one hour. The solution was heated to reflux and allowed to stir an additional 2 h. The mixture was cooled (ice bath) and aqueous sulfuric acid (50 cm^3, H_2SO_4–H_2O, 1 : 2) was added dropwise to the stirred mixture under a blanket of nitrogen. Diethyl ether (100 cm^3) was added and the ethereal solution decanted from the solid salts. The salts were washed with ether (3 × 100 cm^3). The combined fractions were washed with aqueous $NaHCO_3$ (200 cm^3, 5%) and dried over $MgSO_4$. The ethereal solution was filtered and concentrated by rotary evaporation and provided 16.6 g (0.085 mol, 90%) of crude ketol as a bright yellow oil. The crude ketol was oxidized with cupric acetate as follows: the crude ketol (16.0 g, 81.2 mmol) was added to a solution composed of glacial acid (125 cm^3), methanol (13 cm^3), water (14 cm^3) and cupric acetate monohydrate (16.2, 82 mmol). The mixture was refluxed for 3 h and then allowed to stand at room temperature for 12 h. The solution was then filtered through Celite and the residue was washed several times with ether. The organic layer was washed with aqueous sodium hydrogen carbonate (5%) until the aqueous layer remained basic to pH paper. The organic layer was then washed with brine (100 cm^3), dried (Na_2SO_4) and the solvent removed under reduced pressure. The dark oil which resulted was purified by passing it through a column of silica gel (petroleum–benzene, eluent) which provided a viscous yellow oil (7.8 g). This material was purified further by vacuum distillation to yield 3.4 g of **7** (21.5%) which was employed directly in the next step. **7**: bp 65–72 °C at 0.3–0.5 mmHg; ν_{max}/cm^{-1} 2955, 1730, 1705, 1450; δ_H(60 MHz; $CDCl_3$) 1.10–2.23 (18 H, m); *m*/*z* (CI) 195 ($M^+ + 1$, 25.9), 97 (100) (Found: M^+, 194.1295. $C_{12}H_{18}O_2$ requires *M*, 194.1307).

Tetramethyl 1,5-(dicyclopentyl)-3,7-dioxo-*cis*-bicyclo[3.3.0]-octane-2,4,6,8-tetracarboxylate 7b

To a solution of dimethyl 3-oxoglutarate **1** (1.74 g, 10 mmol) in methanol (15 cm^3), solid sodium hydroxide (0.40 g) was added. The mixture was heated to reflux, followed by addition of 1,2-di(cyclopentyl)ethane-1,2-dione **7** in one portion. The heat was removed and the reaction mixture was allowed to stir at room temperature for 70 h. The methanol was then removed under reduced pressure, and the light brown residue was dissolved in water. This aqueous solution was brought to slightly acidic pH with cold aqueous HCl (10%), followed by extraction with chloroform. The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure to provide a viscous oil (3.29 g). Chromatography on silica gel (benzene–EtOAc eluent) of this material yielded a white solid **7b** (0.30 g, 12%). This material was recrystallized from methanol to provide an analytical sample of **7b**, mp 177–179 °C; ν_{max}/cm^{-1} (KBr) 3480, 1750, 1712, 1655; δ_H(60 MHz; $CDCl_3$) 0.8–2.4 (18 H, m), 3.0–3.6 (4 H, br), 3.6–3.8 (12 H); *m*/*z* 507 ($M^+ + 1$, 100%) (Found: M^+, 506.2132. $C_{26}H_{34}O_{10}$ requires *M*, 506.2151). When this reaction was repeated under conditions analogous to those described above, with the exception of the period of time required for heating (2 h reflux in this experiment), a 14% yield of the 1 : 2 adduct **7b** was realized, as well as the recovery of starting dione (12%). At no time was any of the 1 : 1 adduct **7a** isolated from the reaction or observed by TLC or spectroscopy, although several attempts to accomplish this were executed.

Preparation of 1,2-di(cyclopent-3-enyl)ethane-1,2 dione 9 (oxidation with Bi_2O_3)

To a three-neck round bottomed flask equipped with a magnetic stirrer, condenser, thermometer and heating mantle was added the di(cyclopentene) ketol **11** (4.06 g, 0.021 mol) and glacial acetic acid (60 cm^3). Bismuth oxide (4.4 g, 0.009 mol) was added and the solution heated to 90 °C. The progress of the reaction was monitored by TLC (silica gel; 25% EtOAc–benzene). Within 20 min, a new spot of higher R_f was observed. The reaction was allowed to stir for 12 h at 90–100 °C. The reaction mixture was cooled and then diluted with ether (40 cm^3) and hexane (40 cm^3). The bismuth salts which precipitated were removed by filtration through Celite. The volume of the filtrate was reduced under vacuum, diluted with ether (300 cm^3) and washed with 10% $NaHCO_3$ until the pH of the aqueous layer remained slightly basic. The ether layer was dried over $MgSO_4$ and the solvents removed under reduced pressure to provide 2.59 g (64%) of crude diketone **9**. The crude product was purified by column chromatography (silica gel; 10% EtOAc–hexane) to provide 2.0 g (52%) of pure **9**: bp 75–79 °C (0.5–0.7 mmHg); ν_{max}/cm^{-1} (neat) 3064, 1708; δ_H(60 MHz; $CDCl_3$) 2.6 (8 H, d, *J* 7, $CH{=}CHCH_2$), 4.0 (2 H, quintet, *J* 7, CH_2CHCH_2), 5.6 (4 H, s); *m*/*z* 191 ($M^+ + 1$, 100%). This material was employed directly in the next step.

2,5-Bis(methoxycarbonyl)-3,4-dicyclohexyl-4-hydroxycyclopent-2-enone 8a

To a solution of sodium hydroxide (0.8 g, 20 mmol) in methanol (16 cm^3), dimethyl 3-oxoglutarate **1** (7.08 g, 40 mmol) was added. The mixture was heated to reflux for 10 min, after which 1,2-di(cyclohexyl)ethane-1,2-dione **8** (4.45 g, 20 mmol), prepared by the method of Stocker,[9] was added in one portion. The heat was removed and the reaction mixture allowed to stir at room temperature for 9 d. The methanol was subsequently

removed under reduced pressure, and the remaining residue dissolved in water, acidified with cold 1 M HCl and extracted with ether. The organic layer was then dried over $MgSO_4$ and concentrated under reduced pressure to provide crude **8a**. This material was purified by column chromatography on silica gel ($CHCl_3$) to provide the pure 1:1 adduct **8a** (3.15 g, 61.1%) and unreacted dione **8** (1.2 g). An analytically pure sample of **8a** was obtained by recrystallization from petroleum, mp 58–61 °C (Found: C, 66.90; H, 8.25. Calc. for $C_{21}H_{30}O_6$: C, 66.68; H, 7.99%); ν_{max}/cm^{-1} 3510, 2945, 1755, 1735, 1700, 1620; δ_C(62.86 MHz; $CDCl_3$) 25.59, 25.80, 26.01, 26.09, 26.23, 26.27, 27.00, 27.22, 30.02, 32.03, 38.28, 44.13, 52.14, 52.97, 57.89, 83.12, 133.39, 164.20, 168.91, 186.28, 193.5; *m/z* (CI) 396 (M^+ + 18, 100%), 379 (M + 1, 95%).

2,5-Bis(methoxycarbonyl)-3,4-di(2-thienyl)-4-hydroxycyclopent-2-enone 19a

Sodium hydroxide (0.470 g, 11.7 mmol) was dissolved in methanol (30 cm^3). This solution was filtered and dimethyl 3-oxoglutarate **1** (1.20 g, 5.86 mmol) was added and the solution allowed to stir at room temperature for 10 min. 2,2′-Thenil **19** (1.5 g, 5.86 mmol) was added to the mixture in one portion and the mixture allowed to stir at room temperature for a total of 8 h. The resulting precipitate was filtered and dried in vacuum to provide 1.95 g of a bright orange salt (mp >250 °C, darkened at 190 °C); ν_{max}/cm^{-1} (KBr) 3531, 3441, 2899, 1711, 1672, 1567, 1543, 1451, 1440. This salt was suspended in a separatory funnel in H_2O (50 cm^3) and CH_2Cl_2 (100 cm^3). Aqueous HCl (10%, 50 cm^3) was added and the mixture shaken until the solid dissolved. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (50 cm^3). The organic phases were combined, dried over $MgSO_4$ and concentrated under reduced pressure to provide **19a** (1.7 g, 76.7%) as a yellow solid, mp 110–112 °C. An analytical sample of **19a** was obtained through recrystallization from EtOAc–hexane; mp 112–113 °C (Found: C, 53.49; H, 3.81. Calc. for $C_{17}H_{14}O_6S_2$: C, 53.96; H, 3.73%); ν_{max}/cm^{-1} (KBr) 3340, 3101, 1751, 1705, 1696, 1686, 1596, 1497; δ_H(250 MHz; $CDCl_3$) 3.72 (3 H, s), 3.82 (1 H, s), 3.84 (3 H, s), 5.42 (1 H, s), 6.71 (2 H, m), 6.98 (1 H, d, *J* 3.5, 9-H), 7.17 (1 H, dd, *J* 1.5, 5, 4-H), 7.53 (1 H, dd, *J* 1.3, 4, 11-H), 7.65 (1 H, dd, *J* 1.3, 4, 2-H); *m/z* (EI) 378 (M^+, 24.5), 360 (24.5), 346 (26.5), 320 (36.7), 319 (100), 289 (22.4), 288 (57.1), 287 (67.3), 267 (26.5), 235 (20), 195 (38.8), 166 (32.7), 111 (51.1) (Found: M^+, 378.0217. $C_{17}H_{14}O_6S_2$ requires *M*, 378.0232).

Attempted preparation of tetramethyl 3,7-dioxo-1,5-di(2-thienyl)-*cis*-bicyclo[3.3.0]octane-2,4,6,8-tetracarboxylate 19b

Dimethyl 3-oxoglutarate **1** (0.78 g, 4.5 mmol) was added to a solution of methanol (20 cm^3) and sodium hydroxide (0.224 g, 5.6 mmol). The mixture was heated to 60 °C (oil bath) and 2,2′-thenil **19** (0.5 g, 2.25 mmol) was added. The mixture was held at 60 °C for 12 h and then allowed to cool to room temperature. The methanol was removed under reduced pressure and the dark residue was dissolved in $CHCl_3$ (100 cm^3) in a separatory funnel and shaken with aqueous HCl (10%, 10 cm^3). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure leaving a dark viscous material. Examination of the reaction mixture by TLC (silica gel, 60% EtOAc–hexane) indicated the presence of dimethyl 3-oxoglutarate **1**, the 1:1 adduct **19a** of 2,2′-thienyl, and baseline material. The ^1H NMR (60 MHz, $CDCl_3$) spectrum of this material consisted of absorptions in the aromatic region of the spectrum (δ 6.7–7.8) and overlapping singlets in the region of ester methyl hydrogens (δ 3.5–4.1); *m/z* (CI) 379 (6.7), 361 (31.1), 347 (8.9), 331 (20.0), 303 (11.1), 289 (6.7), 175 (4.4), 143 (100). The molecular ion of the desired 1:2 adduct (*m/z* 353) was not present nor were the characteristic fragment ions which would result from the successive losses of methanol from the parent ion observed on mass spectroscopy of this material.

2,5-Bis(methoxycarbonyl)-3,4-di(2-pyridyl)-4-hydroxycyclopent-2-enone 16a

A solution of sodium methoxide was prepared by dissolving sodium metal (0.24 g, 10.4 mmol) in dry methanol (50 cm^3). Dimethyl 3-oxoglutarate **1** (1.82 g, 10.5 mmol) was added and the solution allowed to stir for 10 min at room temperature. The 2,2′-pyridil analog **16** was added in one portion, and immediately dissolved to provide a dark yellow–brown colored solution. Within 20 min, a green–yellow precipitate began to form. The solution was stirred for 12 h, and the resulting solid was filtered from the medium and dried to provide **16a** (2.79 g) as its sodium salt. This material decomposed at 230 °C without melting. The salt **16a** was then dissolved in water (50 cm^3), the pH adjusted to 7.0, and the neutral solution extracted with $CHCl_3$ (3 × 50 cm^3). The combined organic fractions were dried over $MgSO_4$ and concentrated under reduced pressure to give the 1:1 adduct **16a** (2.4 g, 67%). An analytical sample was obtained through recrystallization from methanol, mp 127–130 °C (Found: C, 61.95; H, 4.27; N, 7.46. Calc. for $C_{19}H_{16}N_2O_6$: C, 61.95; H, 4.39; N, 7.61%); ν_{max}/cm^{-1} (KBr) 3400–3000, 1760–1745, 1715; *m/z* (CI) 369 (M^+ + 1, 55.7), 353 (29.7), 351 (11.0), 337 (17.3), 321 (34.0), 311 (100) (Found: M^+, 368.1008. $C_{19}H_{16}N_2O_6$ requires *M*, 368.1008).

2,4,6,8-Tetramethyl 3,7-dioxo-1,5-(biphenyl-2,2′-diyl)-*cis*-bicyclo[3.3.0]octane-2,4,6,8-tetracarboxylate 13b

Sodium hydroxide (3.8 g, 96 mmol) was dissolved in dry methanol (300 cm^3) and dimethyl 3-oxoglutarate **1** (8.36 g, 48 mmol) was added. The solution was heated to 60 °C (oil bath) and phenanthrenequinone **13** (4.0 g, 19.0 mmol) was added. The mixture was then stirred at 60 °C for 2 d. The solution was cooled to room temperature and the precipitate which formed was filtered from the medium, dissolved in water (100 cm^3) and acidified to pH 3 with aqueous HCl (10%). The precipitate was filtered and dried *in vacuo* to yield **13b** (1.7 g) as a cream colored solid. The original filtrate was concentrated under reduced pressure, dissolved in water (100 cm^3), brought to pH 3 and filtered to provide an additional 3.7 g of **13b**. The combined yield (5.4 g) of **13b** was 54%. An analytical sample of **13b** was obtained by recrystallization from $CHCl_3$–hexane, mp 234–235 °C; ν_{max}/cm^{-1} (KBr) 3428, 3071, 1746, 1652, 1619; δ_H(250 MHz; $CDCl_3$) 2.90 (6 H, s), 4.00 (6 H, s), 4.70 (2 H, s), 7.24–7.27 (4 H, t), 7.63–7.67 (2 H, t), 7.73–7.77 (2 H, t), 11.3 (2 H, s, broad enol absorptions); δ_C(62.86 MHz; $CDCl_3$) 51.68, 52.20, 59.18, 108.51, 122.92, 127.84, 128.14, 128.34, 131.40, 135.52, 167.96, 170.69, 175.84; *m/z* (CI, CH_4) 549 (M^+ + 29, 5.6), 521 (M^+ + 1, 26.6), 489 (67.2), 485 (16.9), 457 (100), 431 (10.9), 425 (16.3), 347 (10.7) (Found: M^+, 520.1366. $C_{28}H_{24}O_{10}$ requires *M*, 520.1369).

Conversion of the 1:1 adduct 13a from phenanthrenequinone 13 into the 1:2 adduct 13b with 1 at 60 °C in methanol

Sodium hydroxide (1.9 g, 4.8 mmol) was dissolved in dry methanol and the solution was heated to 60 °C. The mixture was stirred at this temperature for 5 min after which **13a** (2.0 g, 6 mmol) was added. Within 10 min a precipitate began to form and this solution was refluxed for 4.5 h and then allowed to cool to room temperature. The solution was filtered, the filtrate reduced in volume (50 cm^3) and brought to pH 3 with cold aqueous HCl (10%). The suspension was filtered and dried *in vacuo* to provide **13b** (1.81 g, 63%) as a tan solid which was recrystallized from $CHCl_3$–hexane to yield 1.65 g (53%) of product as an off white solid, mp 234–235 °C. This material proved to be identical to an authentic sample of **13b** by comparison of mass and IR spectra, as well as TLC.[25]

1,5-(Biphenyl-2,2′-diyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione 22

The tetraester **13b** (0.454 g, 0.87 mmol) was added to a mixture

of acetic acid (30 cm^3) and aqueous HCl (10%, 30 cm^3). The mixture was heated to reflux and within 1 h the solid dissolved to provide a homogeneous solution which was refluxed for 18 h then cooled to room temperature. Upon cooling, crystals precipitated from the light yellow solution. This solution was cooled to 0 °C (ice bath) and was filtered to provide 204 mg of crystalline **22**. The filtrate was extracted with $CHCl_3$ (3 × 20 cm^3), and the combined organic layers dried over $MgSO_4$ and concentrated under reduced pressure to give an additional 30 mg of **22** (93%). A sample of **22** was obtained by recrystallization from EtOAc–hexane; mp 220–222 °C; ν_{max}/cm^{-1} (KBr) 1725; *m/z* (CI, CH_4) 328 (M^+ + 41, 7.8), 317 (M^+ + 29, 14.9), 289 (M^+ + 1, 75.7), 231 (100); δ_H(250 MHz; $CDCl_3$) 2.62 (4 H, d, *J* 19.4, CH_2 *endo*), 2.93 (4 H, d, *J* 19.4, CH_2 *exo*), 7.92 (2 H, m), 7.35 (6 H, m); δ_C(62.86 MHz; $CDCl_3$) 50.00, 50.64, 124.56, 127.80, 128.30, 128.97, 131.09, 136.2, 214.04 (Found: M^+, 288.1129. $C_{20}H_{16}O_2$ requires M^+, 228.1150).

Reaction of ethyl 2,3-dioxopropionate with dimethyl 3-oxoglutarate to provide tetramethyl 5,7-dihydroxy-2-oxo-2,3-dihydro-1*H*-indene-1,3,4,6-tetracarboxylate 25 and tetramethyl 1-ethoxycarbonyl-3,7-dihydroxybicyclo[3.3.0]octa-2,6-diene-2,4,6,8-tetracarboxylate 24

Dimethyl 3-oxoglutarate **1** (5.22 g, 0.03 mol) was dissolved in aqueous sodium hydrogen carbonate buffer (1.4 g $NaHCO_3$ in 100 cm^3 H_2O) and ethyl 2,3-dioxopropionate[27] **23** (2.22 g, 0.015 mol) was then added in one portion. This mixture was allowed to stir for 4 d and then acidified to pH 1 with ice-cold 6 M aqueous HCl. The water layer was extracted with $CHCl_3$ (3 × 50 cm^3). The combined extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure to provide an oil which was dissolved in ethanol and allowed to crystallize. The crystals were filtered from the solution and dried to furnish **25** (2.08 g, 35%) as a white crystalline solid, mp 173–175 °C (Found: C, 51.33; H, 4.01. Calc. for $C_{17}H_{16}O_{11}$: C, 51.52; H, 4.04%); ν_{max}/cm^{-1} (KBr) 3373, 2955, 1772, 1739, 1665; δ_H(250 MHz; $CDCl_3$) major isomer 3.72 (3 H, s), 3.74 (3 H, s), 3.85 (3 H, s), 4.01 (3 H, s), 4.46 (1 H, s), 4.78 (1 H, s), 12.63 (1 H, s), 12.93 (1 H, s); δ_C(62.86 MHz; $CDCl_3$) 52.10, 53.01, 53.09, 56.48, 62.98, 63.11, 102.05, 102.42, 118.08, 118.38, 144.34, 144.50, 164.45, 165.47, 166.01, 166.52, 166.74, 169.92, 171.10, 199.59, 199.89; *m/z* 397 (18.6, M^+ + 1). The mother liquor was evaporated slowly to provide **24** as a white crystalline solid (1.72 g, 26%), mp 121–123 °C; ν_{max}/cm^{-1} (KBr) 3286, 2956, 1735, 1677; δ_H(250 MHz; $CDCl_3$) 1.21 (3 H, t, *J* 9, CH_3CH_2), 3.61 (3 H, s), 3.71 (3 H, s), 3.72 (1 H, d, *J* 7, 5-H), 3.77 (3 H, s), 3.84 (3 H, s), 3.91 (1 H, d, *J* 7, 4-H), 4.22 (2 H, q, *J* 9, CH_3CH_2), 4.62 (1 H, s), 10.12 (1 H, s), 10.55 (1 H, s); *m/z* (CI, CH_4) 443 (M^+ + 1, 78.4%).

Reaction of 25 with CH_2N_2[28] to provide 2,5,7-trimethoxy-1,3,4,6-tetramethoxycarbonylindene 27 and 1-methyl-2,4,6-trimethoxy-1,3,5,7-tetramethoxycarbonylindene 28

The indene **25** (1 g, 2.53 mmol) (enol form, see **26**) was added to a 50 cm^3 (0.67 M) ether solution of CH_2N_2 at 0 °C. The mixture was stirred at 0 °C for 2 h and then stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (silica gel; hexane–EtOAc = 1:2) to furnish **27** (0.69 g, 62.4%) and **28** (0.27 g, 23.7%). Indene **27**, mp 154–155 °C (Found: C, 54.78; H, 5.01. Calc. for $C_{20}H_{22}O_{11}$: C, 54.79; H, 5.02%); ν_{max}/cm^{-1} (KBr) 2952, 1735; δ_H(250 MHz; $CDCl_3$) 3.72 (3 H, s), 3.83 (3 H, s), 3.87 (3 H, s), 3.88 (3 H, s), 3.89 (3 H, s), 3.92 (3 H, s), 4.03 (3 H, s), 4.59 (1 H, s); δ_C(62.86 MHz; $CDCl_3$) 51.58, 51.84, 52.14, 52.43, 52.90, 59.79, 60.67, 64.25, 111.66, 112.36, 116.24, 120.67, 145.18, 153.62, 157.90, 163.64, 165.93, 165.99, 167.71, 167.90; *m/z* (CI) 439 (46, M^+ + 1). Indene **28**, mp 136–137 °C (Found: C, 55.66; H, 5.27. Calc. for $C_{21}H_{24}O_{11}$: C, 55.75; H, 5.31%); ν_{max}/cm^{-1} (KBr) 2950, 1735; δ_H(250 MHz; $CDCl_3$) 1.50 (3 H, s), 3.62 (3 H, s), 3.64 (3 H, s), 3.67 (3 H, s), 3.77 (3 H, s), 3.91 (3 H, s), 3.92 (3 H, s), 3.94 (3 H, s); δ_C(62.86 MHz; $CDCl_3$) 18.64, 51.90, 52.47, 58.72, 59.66, 62.61, 63.98, 104.49, 118.89, 123.04, 131.32, 142.59, 154.42, 163.66, 165.31, 166.06, 167.00, 170.16; *m/z* (CI) 453 (46, M^+ + 1).

Reaction of indene 27 with CH_2N_2 to provide indene 28

Indene **27** (20 mg, 0.0457 mmol) was added to 8 cm^3 of an ether solution of CH_2N_2 (0.67 M) at 0 °C. The mixture was stirred at 0 °C for 2 h and was then stirred at room temp. for 4 h. The solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel; EtOAc–hexane = 2:3) to give **28** (17.5 mg, 85%) which was identical with **28** obtained in the previous experiment.

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