The Chemistry of Aryl-lead(IV) Tricarboxylates. Reaction with Vinylogous β-Keto Esters

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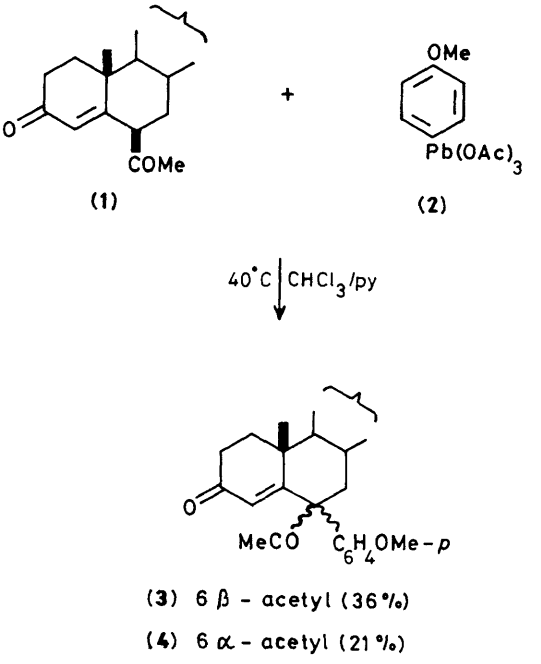
A study of the arylation of ethyl 4-oxocyclohex-2-enecarboxylate and a number of its derivatives by aryl-lead triacetates has been carried out. Ethyl 2-methyl-4-oxocyclohex-2-enecarboxylate (Hagemann's ester) (**7**), and ethyl 4-oxocyclohex-2-enecarboxylate (**10a**) and its double bond isomer (**10b**) were found to undergo regiospecific arylation at C-1 in good yield, whereas the compounds (**14**) and (**16**), which have C-3 substituents, gave low yields of products resulting from arylation at both C-1 and C-3. The latter behaviour was also displayed by the isomers (**20a**) and (**20b**), which contain a 6-methyl substituent.

In recent years two groups of organometallic compounds have been shown to be particularly useful aryl cation equivalents which may effect the arylation of a variety of carbon and other nucleophiles under quite mild conditions. These are aryl-bismuth(V) compounds, which are being studied by Barton,[1] and aryl-lead(IV) compounds, which we are investigating.[2] Our work has been confined mainly to aryl-lead triacetates, which have been shown to affect the *C*-arylation of phenols,[3] β-dicarbonyls,[4] α-cyano esters,[5] enamines,[6] and nitroalkanes.[7]

Although we have devoted much of our study to β-dicarbonyl compounds, in only one case was this extended to include a vinologue. This involved a brief investigation of the reaction of 6β-acetylcholest-4-en-3-one (**1**) with *p*-methoxyphenyl-lead triacetate (**2**),[8] which proceeded slowly but cleanly to give a mixture of 6α- and 6β-*p*-methoxyphenyl derivatives (**3**) and (**4**) (Scheme 1). Interestingly, there was no evidence for attack occurring at the alternative site, C-4. In order to extend our knowledge of the regiochemistry of this arylation reaction of vinylogous β-dicarbonyls, we undertook an investigation of the reactions of ethyl 2-methyl-4-oxocyclohex-2-enecarboxylate (Hagemann's ester) (**7**) and a number of closely related compounds with aryl-lead triacetates, and we now report the details of that study.[9]



Scheme 1.

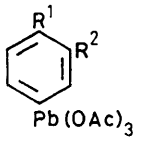
Discussion

From the results, which are summarised in the Table, it can be seen that Hagemann's ester (**7**) underwent reaction with both *p*-methoxyphenyl-lead triacetate (**2**) (entries 1 and 2) and phenyl-lead triacetate (**5**) (entry 3) to give only the products of arylation at C-1, the keto esters (**8**) and (**9**) respectively, in synthetically useful yields. No products of attack at the alternative site, C-3, could be detected by n.m.r. spectroscopy. The conditions employed in this work require some comment. In the past we have generally not used temperatures above 40 °C for reactions of aryl-lead triacetates to avoid the possibility of homolytic

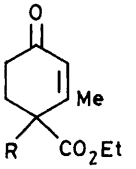
Table. Reaction of ethyl 4-oxocyclohex-2-enecarboxylate and derivatives with aryl-lead triacetates

Entry	Keto ester	$ArPb(OAc)_3$ [a]	Solvent	Base [b]	Temp (°C)	Time (h)	Products, yield
1	(**7**)	(**2**)	$CHCl_3$	py	40	72	(**8**)53
2	(**7**)	(**2**)	$CHCl_3$	py	60	48	(**8**)88
3	(**7**)	(**5**)	DMSO		40	24	(**9**)59
4	(**10a**) (**10b**)	(**2**)	$CHCl_3$	py	55	24	(**11**)70
5	(**10a**) (**10b**)	(**2**)	DMSO		40	48	(**11**)68
6	(**10a**) (**10b**)	(**5**)	$CHCl_3$	py	60	48	(**12**)60
7	(**10a**) (**10b**)	(**6**)	DMSO		40	48	(**13**)53
8	(**14**)	(**2**)	$CHCl_3$	DMAP	60	48	(**15**)3, (**18**)5
9	(**16**)	(**2**)	$CHCl_3$	py	60	48	(**17**)3, (**19**)9
10	(**20a**) (**20b**)	(**2**)	$CHCl_3$	DMAP	60	48	(**21**)9, (**22**)1, (**23**)1

[a] The ratio of keto ester:$ArPb(OAc)_3$ was 1:1.5 for entries 1 and 3, 1:1.2 for entries 2 and 4, and 1:2 for entries 5—10. [b] The ratio of substrate to pyridine (py) or 4-(*N*,*N*-dimethylamino)pyridine (DMAP) was 1:3.

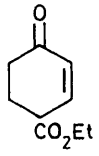


(2) R^1 = OMe, R^2 = H
(5) R^1 = R^2 = H
(6) R^1 = R^2 = OMe

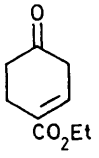


(7) R = H
(8) R = *p*-$MeOC_6H_4$
(9) R = Ph

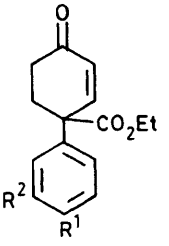
cleavage. However, with the present substrates there was no evidence of this at 60 °C, and a considerable improvement in the rate of reaction, and in the yield of compound (**8**), was achieved at this temperature in chloroform containing pyridine (entry 2). A similar effect was observed at the lower temperature (40 °C) by using dimethyl sulphoxide in place of chloroform–pyridine, but here a less satisfactory isolation procedure affected the yields. The parent substrate, ethyl 4-oxocyclohex-2-enecarboxylate (**10a**), which is obtained as an equilibrium mixture with its double-bond isomer (**10b**) and for which an improved synthesis is reported below, also underwent regiospecific arylation at C-1 with lead compounds (**2**), (**5**), and (**6**) (entries 4—7) to give the keto esters (**11**), (**12**), and (**13**) respectively. As noted previously,[9] the products (**11**) and (**13**) are potentially useful intermediates for the synthesis of the alkaloids (±)-*O*-methyljoubertiamine and (±)mesembrine respectively.



(10a)



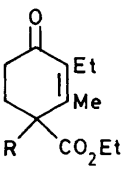
(10b)



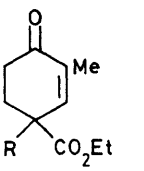
(11) R^1 = OMe, R = H
(12) R^1 = R^2 = H
(13) R^1 = R^2 = OMe

In previous work with simple β-dicarbonyl compounds, we had noted that their reactions with aryl-lead triacetates were faster and generally cleaner when the compound contained one replaceable hydrogen. Examples of this behaviour are to be found in the low reactivity of ethyl acetoacetate,[10] diethyl malonate,[4] and Meldrum's acid.[4] Although two such dicarbonyls, dimedone[8] and barbituric acid,[4] have been found to give high yields of products of diarylation, the second arylation is clearly faster than the first, since none of the intermediate mono-aryl compound could be obtained. It was therefore of interest to examine derivatives of (**10a**) containing a substituent at C-3. The two compounds selected were the readily available Hagemann's ester derivative (**14**) and ethyl 3-methyl-4-oxocyclohex-2-enecarboxylate (**16**), a synthesis of which is given in Scheme 3.

Both 3-substituted compounds, (**14**) and (**16**), were considerably less reactive than Hagemann's ester (**7**) and the mixture of (**10a**) and (**10b**) towards the aryl-lead compound (**2**), and for the reaction of the former compound it was necessary to use 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in place of pyridine to increase the rate of reaction. Although with (**14**) and (**16**) the yields of aryl-substituted products were low, in both cases attack occurred at both C-1 and C-3 (entries 8 and 9 respectively), thus reinforcing our view that the arylation of β-

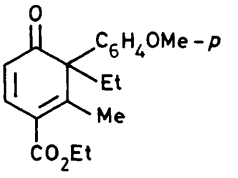


(14) R = H
(15) R = *p*-$MeOC_6H_4$

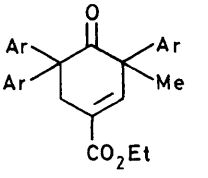


(16) R = H
(17) R = *p*-$MeOC_6H_4$

dicarbonyls is favoured at more substituted sites, provided, of course, steric inhibition is not a complicating factor. The reaction of compound (**14**) at C-1 yielded the expected keto ester (**15**); however, the product resulting from arylation at C-3 was the dienone (**18**), which can be rationalized as arising by



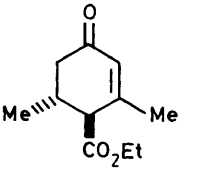
(18)



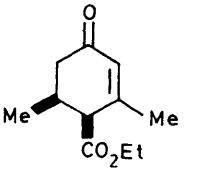
(19) Ar = *p*-$MeOC_6H_4$

oxidation of the initially formed arylated keto ester. A precedent for this introduction of a double bond by an aryl-lead triacetate is to be found in the formation of an enedione from a 1,4-diketone in one of our earlier studies.[8] As with the previous substrates, the 3-methyl derivative (**16**) underwent arylation at C-1 to give an α,β-unsaturated ketone (**17**), but like compound (**14**) the initial product of attack at C-3 underwent further reaction. In this case diarylation at C-5 occurred to produce the 3,5,5-triaryl compound (**19**).

In view of the marked influence which a C-3 substituent had on the arylation of this system, it was of interest to examine the effect of substituents at other positions of the cyclohexenone ring. One previously reported compound,[11] which was readily obtained, was ethyl 2,6-dimethyl-4-oxocyclohex-2-enecarboxylate. The ^{1}H n.m.r. spectrum of this material showed it to be, in fact, a 2:1 mixture of the *trans* and *cis* isomers (**20a**) and (**20b**) respectively. This was readily determined by the appearance of the signal for 1-H, which was a broad doublet for each isomer, with a coupling constant of *ca.* 8 Hz for the *trans*-isomer and 4 Hz for the *cis*-isomer. The results of the reaction of *p*-methoxyphenyl-lead triacetate (**2**) with the mixture of isomers (**20a**) and (**20b**), which are included in the Table (entry 10), are

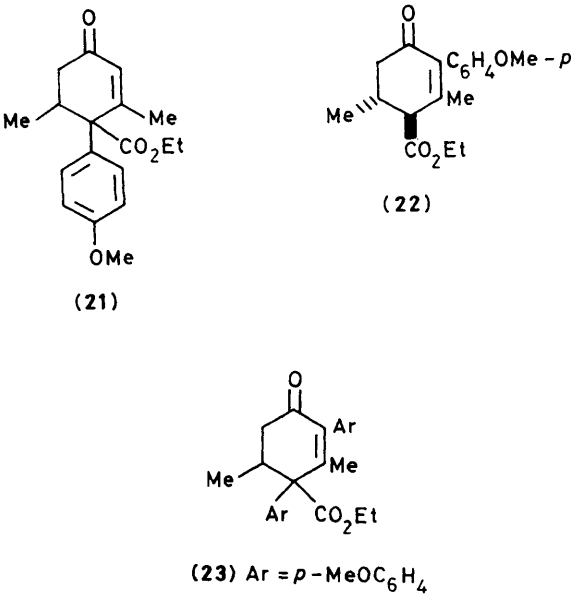


(20a)



(20b)

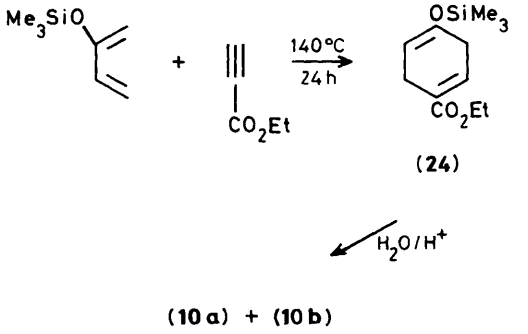
further evidence of the sensitivity of the arylation reaction of this system to minor structural changes. The more forcing conditions employed for substrate (**14**) were required for a satisfactory reaction rate, and the crude product contained at least five products (t.l.c.). Three of these could be separated by h.p.l.c. and were shown (see Experimental section) to have the structures (**21**)—(**23**). The stereochemistry could not be assigned to compounds (**21**) and (**23**); however, in the case of



(**22**), the broad doublet due to 1-H in the n.m.r. spectrum had a coupling constant of *ca.* 8 Hz, indicating that it had the same stereochemistry as isomer (**20a**), *i.e. trans.*

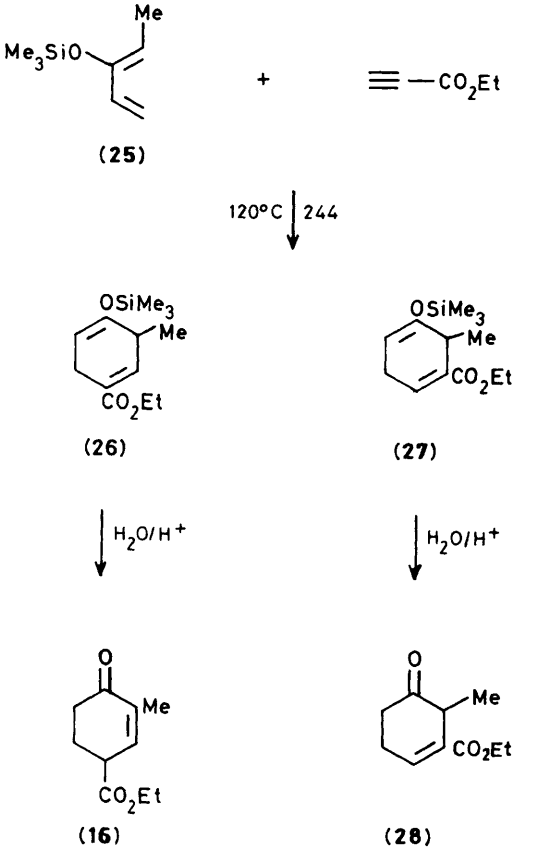
It would appear likely that the low yield of the expected compound (**21**), and the formation of products resulting from arylation at C-3, is due to steric hindrance to reaction at C-1 by the 6-methyl group. Compound (**22**) no doubt arises by arylation at C-3 followed by migration of the double bond into conjugation; this product may then undergo further arylation at C-1 to yield the 1,3-diaryl derivative (**23**).

Synthesis of Keto Esters.—It had previously been reported[12] that the Diels–Alder reaction of 2-ethoxybuta-1,3-diene and ethyl propiolate, followed by an aqueous acid hydrolysis of the adduct, afforded the keto ester (**10b**). Since we found the conversion of methyl vinyl ketone into 2-trimethylsilyloxybuta-1,3-diene[13] a more efficient procedure than the preparation of the 2-ethoxy derivative,[14] we used this compound in the Diels–Alder reaction. This gave rise to ethyl 4-trimethylsiloxycyclohexa-1,4-dienecarboxylate (**24**) in 77% yield (Scheme 2).



Scheme 2.

Aqueous acid hydrolysis of the enol ether (**24**) afforded a quantitative yield of material which corresponded to that reported by Logothetis and Nelson,[12] but was clearly a mixture consisting of 25% of isomer (**10a**) and 75% of (**10b**), on the grounds of the ^{1}H n.m.r. spectrum. The signal due to 3-H of



Scheme 3.

isomer (**10a**) appeared as a doublet of doublets at δ 6.07, while that for 2-H of (**10b**) was a triplet of triplets at 7.01.

Although the synthesis of ethyl 3-methyl-4-oxocyclohex-2-enecarboxylate (**16**) had been briefly reported,[15] we explored the possibility of employing the readily available ethyl vinyl ketone in a route analogous to that used above (see Scheme 3). This involved its conversion into 3-trimethylsiloxypenta-1,3-diene (**25**), which was then heated with ethyl propiolate in benzene at 120 °C. The Diels–Alder reaction, however, was non-regiospecific, yielding a mixture of the two possible adducts, ethyl 3-methyl-4-trimethylsiloxycyclohexa-1,4-dienecarboxylate (**26**) and ethyl 6-methyl-5-trimethylsiloxycyclohexa-1,4-dienecarboxylate (**27**) in a 10:7 ratio in low isolated yield. Since these dienes were unstable at room temperature, the crude mixture was hydrolysed in aqueous acid, and the resulting material was separated by h.p.l.c. to yield ethyl 3-methyl-4-oxocyclohex-2-enecarboxylate (**16**) and ethyl 6-methyl-5-oxocyclohex-1-enecarboxylate (**28**) in a 7:6 ratio and total overall yield of 13%.

Experimental

The instruments employed for spectroscopic determinations and general procedures have been noted previously,[16] except that h.p.l.c. was carried out on a Whatman Partisil M20 10/50 column at a flow rate of 13 ml min^{-1}, using refractive index and ultraviolet (280 nm) detectors. Previously reported methods were used to prepare phenyl-lead triacetate,[17] *p*-methoxyphenyl-lead triacetate,[18] and 3,4-dimethoxyphenyl-lead triacetate.[17] Hagemann's ester (**7**) and ethyl 3-ethyl-2-methylcyclohex-2-enecarboxylate (**14**) were purchased from Aldrich Chemical Company.

Synthesis of a Mixture of Ethyl 4-Oxocyclohex-2-enecarboxylate (**10a**) *and the Isomer* (**10b**).—A mixture of 2-trimethylsiloxybuta-1,3-diene[13] (11.57 g, 8.14 mmol), ethyl propiolate (7.98 g, 8.14 mmol), anhydrous benzene (85 ml), and hydroquinone (0.03 g) was heated in an autoclave at 140 °C for 24 h. The benzene was removed and the residue was distilled to yield *ethyl 4-trimethylsiloxycyclohexa-1,4-dienecarboxylate* (**24**) (15.15 g, 77.3%) as a colourless liquid, b.p. 120—125 °C at 1.0 mmHg (Found: C, 60.3; H, 8.7. $C_{12}H_{20}O_3Si$ requires C, 60.0; H, 8.4%); $\nu_{max.}$(film) 1 720 and 1 688 cm^{-1}; $\lambda_{max.}$(MeOH) 227 and 250sh nm (ε 1 780 and 813); $\delta_H(CDCl_3)$ 0.22 (9 H, s, $SiMe_3$), 1.30 (3 H, t, *J* 7.0 Hz, Me), 2.92 (4 H, m, 2 × CH_2), 4.19 (2 H, q, *J* 7.0 Hz, CH_2), 4.90 (1 H, m, 5-H), and 6.91 (1 H, m, 2-H); *m/z* 240 (*M*, 37%), 211 (*M* − Et, 26), 167 (*M* − CO_2Et, 26), and 151 (*M* − $OSiMe_3$, 40).

A solution of the silyl enol ether (**24**) (15.1 g) in a mixture of tetrahydrofuran (37 ml), water (30 ml), and sulphuric acid (6.5 ml) was stirred at room temperature for 1 h. Water (100 ml) was added and the product was isolated by extraction with ether (2 × 100 ml). Fractional distillation of the resulting oil gave a 1:3 mixture of ethyl 4-oxocyclohex-2-enecarboxylate (**10a**) and ethyl 4-oxocyclohex-1-enecarboxylate (**10b**) as a colourless oil (77% overall yield when intermediate not purified), b.p. 83—85 °C at 0.3 mmHg (lit.,[12] 83—84.5 °C at 0.3 mmHg); $\delta_H(CDCl_3)$ for (**10a**) 1.30 (3 H, t, Me), 2.0—2.9 (4 H, m, 2 × CH_2), 3.40 (1 H, m, 1-H), 4.22 (2 H, q, CH_2), 6.07 (1 H, dd, $J_{2,3}$ 10.3 Hz, $J_{1,3}$ 2.5 Hz, 3-H), and 7.16 (1 H, m, 2-H); $\delta_H(CDCl_3)$ for (**9b**) 1.28 (3 H, t, Me), 2.0—2.9 (4 H, m, 2 × CH_2), 2.9—3.25 (2 H, m, 2 × 3-H), 4.23 (2 H, q, CH_2), and 7.01 (1 H, tt, $J_{2,3}$ 4.0 Hz, $J_{2,6}$ 1.2 Hz).

3-Trimethylsiloxypenta-1,3-diene (**25**).—Chlorotrimethylsilane (32.6 g, 0.30 mol) was added dropwise to a stirred solution of ethyl vinyl ketone (21.03 g, 0.25 mol) in dimethylformamide (100 ml) and triethylamine (60.6 g, 0.6 mol) under nitrogen. The mixture was heated at 80 °C for 5 h and then kept overnight at room temperature. Pentane (200 ml) was added and the mixture was washed with cold aqueous sodium hydrogen carbonate (5%; 3 × 300 ml). The combined aqueous extracts were washed with pentane (200 ml) and this was added to the initial extract. The pentane solution was then washed rapidly with cold hydrochloric acid (1.5M; 100 ml) and cold aqueous sodium hydrogen carbonate (5%; 100 ml), dried (Na_2SO_4), and evaporated. The crude product was distilled to give the *title compound* (**25**) (13.3 g, 34%) as a colourless liquid, b.p. 25—28 °C at 3 mmHg (Found: C, 62.0; H, 10.6. $C_8H_{16}OSi$ requires C, 61.5; H, 10.3%); $\nu_{max.}$(film) 1 605 cm^{-1}; $\lambda_{max.}$(EtOH) 235 nm (ε 9 700); $\delta_H(CDCl_3)$ 0.23 (9 H, s, $SiMe_3$), 1.66 (3 H, dd, $J_{4,5}$ 7.3 Hz, $J_{2,5}$ 0.85 Hz, 3 × 5-H), 4.90 (1 H, dq, $J_{4,5}$ 7.3 Hz, $J_{2,4}$ 0.85 Hz, 4-H), 4.94 (1 H, ddq, $J_{1,2cis}$ 10.5 Hz, J_{gem} 1.7 Hz, $J_{1,4}$ 0.7 Hz, 1-H), 5.24 (1 H, ddq, $J_{1,2trans}$ 17.0 Hz, J_{gem} 1.7 Hz, $J_{1,4}$ 0.7 Hz, 1-H), and 6.18 (1 H, dddq, $J_{1,2trans}$ 17.0 Hz, $J_{1,2cis}$ 10.5 Hz, $J_{2,4}$ 0.85 Hz, $J_{2,5}$ 0.85 Hz, 2-H).

Reaction of 3-Trimethylsiloxypenta-1,3-diene with Ethyl Propiolate.—A mixture of 3-trimethylsiloxypenta-1,3-diene (**25**) (7.90 g, 50.5 mmol), ethyl propiolate (4.96 g, 50.5 mmol), anhydrous benzene (53 ml), and hydroquinone (0.02 g) was heated in an autoclave at 120 °C for 24 h. The benzene was removed and the crude product was fractionated by p.l.c. using light petroleum–ether (88:12) and then by h.p.l.c. using light petroleum–ethyl acetate (99:1) as the eluting solvent.

The less polar material was *ethyl 6-methyl-5-trimethylsiloxycyclohexa-1,4-dienecarboxylate* (**27**) (1.29 g, 10%), obtained as a colourless liquid (Found: C, 60.9; H, 8.1. $C_{12}H_{22}O_3Si$ requires C, 61.4; H, 8.7%); $\nu_{max.}$(film) 1 715 cm^{-1}; $\lambda_{max.}$(EtOH) 292 nm (ε 1 096); $\delta_H(CDCl_3)$ 0.21 (9 H, s, $SiMe_3$), 1.22 (3 H, d, *J* 6.7 Hz, 6-Me), 1.30 (3 H, t, *J* 7.0 Hz, Me), 2.85—2.95 (2 H, m, 2 × 3-H), 3.06 (1 H, q, *J* 6.7 Hz, 6-H), 4.22 (2 H, q, *J* 7.0 Hz, CH_2), 4.74 (1 H, m, 4-H), and 6.91 (1 H, m, 2H); *m/z* 254 (*M*, 24%) and 181 (*M* − $SiMe_3$, 64).

The more polar fraction afforded *ethyl 3-methyl-4-trimethylsiloxycyclohexa-1,4-dienecarboxylate* (**26**) (0.84 g, 7%), as a colourless liquid (Found: C, 61.6; H, 8.6. $C_{13}H_{22}O_3Si$ requires C, 61.4; H, 8.7%); $\nu_{max.}$(film) 1 710 and 1 595 cm^{-1}; $\lambda_{max.}$(EtOH) 257 nm (ε 5 500); $\delta_H(CDCl_3)$ 0.22 (9 H, s, $SiMe_3$), 1.19 (3 H, d, *J* 6.0 Hz, 3-Me), 1.29 (3 H, t, *J* 7.0 Hz, Me), 2.56 (1 H, q, *J* 6.0 Hz, 3-H), 2.95—3.02 (2 H, m, 2 × 6-H), 4.20 (2 H, q, *J* 7.0 Hz, CH_2), 4.83 (1 H, m, 5-H), and 6.80 (1 H, m, 2-H); *m/z* 254 (*M*, 21%) and 239 (*M* − Me, 48).

The crude reaction product, from a second reaction between the enol ether (**25**) and ethyl propiolate conducted as above, was treated in tetrahydrofuran (40 ml) with dilute sulphuric acid (3M; 50 ml), and the mixture was stirred at room temperature for 2 h. Water (100 ml) was added and the product was isolated by means of ether (2 × 100 ml) in the usual way. The crude material was initially fractionated by p.l.c. using light petroleum–ether (1:1), and the two major products were further purified by h.p.l.c. using light petroleum–ethyl acetate (93:7) as the eluting solvent. The less polar compound was *ethyl 6-methyl-5-oxocyclohex-1-enecarboxylate* (**28**) (0.58 g, 6%), a colourless liquid (Found: M^+, 182.092. $C_{10}H_{14}O_3$ requires M^+, 182.094); $\nu_{max.}$(film) 1 720, 1 704, and 1 645 cm^{-1}; $\delta_H(CDCl_3)$ 1.31 (3 H, d, *J* 7.0 Hz, 6-Me), 1.32 (3 H, t, *J* 7.0 Hz, Me), 2.29—2.73 (4 H, m, 2 × CH_2), 3.26 (1 H, q, *J* 7.0 Hz, 6-H), 4.23 (2 H, q, *J* 7.0 Hz, CH_2), and 7.11 (1 H, m, 2-H); $\delta_C(CDCl_3)$ 14.02 (q, Me), 17.79 (q, Me), 24.87 (t, CH_2), 35.06 (t, CH_2), 42.98 (d, C-6), 60.38 (t, OCH_2), 134.02 (s, C-1), 137.13 (d, C-2), 165.31 (s, CO_2), and 211.16 (s, C-5).

The more polar material was *ethyl 3-methyl-4-oxocyclohex-2-enecarboxylate* (**16**) (0.65 g, 7%), a colourless liquid with b.p. 95 °C at 0.02 mmHg (Found: M^+, 182.0948; C, 65.6; H, 7.8; $C_{10}H_{14}O_3$ requires M^+, 182.0943; C, 65.9; H, 7.7%); $\nu_{max.}$ 1 730 and 1 675 cm^{-1}; $\lambda_{max.}$(EtOH) 233 nm (ε 7 950); $\delta_H(CDCl_3)$ 1.30 (3 H, t, *J* 7.0 Hz, Me), 1.82 (3 H, dd, *J* 1.5 Hz, *J* 1.6 Hz, 3-Me), 2.08—2.74 (4 H, m, 2 × CH_2), 3.37 (1 H, m, 1-H), 4.21 (2 H, q, *J* 7.0 Hz, CH_2), and 6.82 (1 H, m, 2-H); $\delta_C(CDCl_3)$ 14.02 (q, Me), 15.24 (q, Me), 25.84 (t, CH_2), 36.36 (t, CH_2), 41.88 (d, C-1), 61.10 (t, OCH_2), 136.42 (s, C-3), 141.29 (d, C-2), 171.86 (s, CO_2), and 198.29 (s, C-4).

Ethyl 1-(p-Methoxyphenyl)-2-methyl-4-oxocyclohex-2-enecarboxylate (**8**).—(*a*) Ethyl 2-methyl-4-oxocyclohex-2-enecarboxylate (**7**) (0.55 g, 3.0 mmol) was added to a solution of *p*-methoxyphenyl-lead triacetate (2.21 g, 4.5 mmol) and pyridine (0.71 g, 9.0 mmol) in chloroform (5.0 ml), and the mixture was stirred at 40 °C for 72 h. Chloroform (50 ml) was added and the solution was washed with sulphuric acid (1.5M; 2 × 25 ml), saturated aqueous sodium hydrogen carbonate (2 × 25 ml), and water (2 × 40 ml). The organic phase was dried ($MgSO_4$), the solvent removed, and the residue was fractionated by flash chromatography using light petroleum–ethyl acetate (70:30) as the eluting solvent. The *title compound* (**8**) (460 mg, 53%) was obtained as an oil (Found: C, 71.0; H, 7.0. $C_{17}H_{20}O_4$ requires C, 70.8; H, 7.0%); $\nu_{max.}$(film) 1 725, 1 670, and 1 615 cm^{-1}; $\lambda_{max.}$(EtOH) 230 nm (ε 18 600); $\delta_H(CDCl_3)$ 1.30 (3 H, t, *J* 7.0 Hz, Me), 1.90 (3 H, d, *J* 1.5 Hz, 2-Me), 2.2—2.9 (4 H, m, 2 × CH_2), 3.80 (3 H, s, OMe), 4.31 (2 H, q, *J* 7.0 Hz, CH_2), 6.12 (1 H, q, *J* 1.5 Hz, 3-H), and 6.90 and 7.10 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H, and 6′-H respectively); *m/z* 288 (*M*, 23%) and 215 (*M* − CO_2Et, 100).

(*b*) The keto ester (**7**) (0.55 g, 3.0 mmol) was added dropwise, with stirring to a solution of *p*-methoxyphenyl-lead triacetate (1.76 g, 3.6 mmol) in chloroform (5 ml) containing pyridine (0.71 g, 9.0 mmol) and the reaction mixture was stirred at 60 °C for

48 h. Work-up as in (*a*) afforded the keto ester (**8**) (761 mg, 88%), identical, (n.m.r. spectrum) with the material obtained above.

Ethyl 2-*Methyl*-1-*phenyl*-4-*oxocyclohex*-2-*enecarboxylate* (**9**).—Ethyl 2-methyl-4-oxocyclohex-2-enecarboxylate (0.55 g, 3.0 mmol) was added dropwise with stirring to phenyl-lead triacetate (**5**) (2.08 g, 4.5 mmol) in dry dimethyl sulphoxide (5 ml) at room temperature, and the mixture was stirred at 40 °C for 48 h. Work-up and chromatography as for the preparation of (**8**) yielded the *title compound* (**9**) (460 mg, 59.4%) as an oil (Found: C, 74.2; H, 7.1. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%); $\nu_{max.}$(film) 1 725 and 1 670 cm^{-1}; $\lambda_{max.}$(EtOH) 234 nm (ε 13 490); $\delta_H(CDCl_3)$ 1.32 (3 H, t, *J* 7.0 Hz, Me), 1.91 (3 H, d, *J* 1.3 Hz, 2-Me), 2.1—3.0 (4 H, m, 2 × CH_2), 4.32 (2 H, q, *J* 7.0 Hz, CH_2), 6.17 (1 H, q, *J* 1.3 Hz, 3-H), and 7.05—7.55 (5 H, m, ArH); *m*/*z* 258 (*M*, 60%) and 185 (*M* − CO_2Et, 100).

Ethyl 1-(p-*Methoxyphenyl*)-4-*oxocyclohex*-2-*enecarboxylate* (**11**).—(*a*) A solution of *p*-methoxyphenyl-lead triacetate (**2**) (1.76 g, 3.6 mmol) in chloroform (5 ml) containing pyridine (0.71 g, 9.0 mmol) was cooled to 0 °C, and the mixture of isomeric keto esters (**10a**) and (**10b**) (0.505 g, 3.0 mmol) was added dropwise with stirring. After 30 min the mixture was heated to 55 °C and stirred for 24 h. The reaction was worked up as in the preparation of (**8**) above to give the *title compound* (**11**) (576 mg, 70%) as an oil (Found: C, 70.1; H, 6.1. $C_{16}H_{18}O_4$ requires C, 70.1; H, 6.6%); $\nu_{max.}$(film) 1 730, 1 685, and 1 605 cm^{-1}; $\lambda_{max.}$(EtOH) 220 nm (ε 13 180); $\delta_H(CDCl_3)$ 1.22 (3 H, t, *J* 7.0 Hz, Me), 2.1—2.9 (4 H, m, 2 × CH_2), 3.78 (3 H, s, OMe), 4.22 (2 H, q, *J* 7.0 Hz, CH_2), 6.20 (1 H, d, *J* 10.0 Hz, 3-H), 6.90 and 7.23 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H and 6′-H respectively), and 7.35 (1 H, d, *J* 10.0 Hz, 2-H); *m*/*z* 274 (*M*, 17%) and 201 (*M* − CO_2Et, 100).

(*b*) The experiment reported in entry 5 of the Table was carried out with the mixture of isomers (**10a**) and (**10b**) (2.78 g, 16.5 mmol) in the same way as outlined above for the synthesis of (**9**), to yield keto ester (**11**) (3.09 g, 68.3%), identical (n.m.r. spectrum) with the material obtained in (*a*) above.

Ethyl 1-*Phenyl*-4-*oxocyclohex*-2-*enecarboxylate* (**12**).—The mixture of keto esters, (**10a**) and (**10b**), (0.505 g, 3.0 mmol) was added dropwise with stirring to a solution of phenyl-lead triacetate (**5**) (2.77 g, 6.0 mmol) in chloroform (5 ml) containing pyridine (0.71 g, 9.0 mmol) at room temperature, and the mixture was then stirred at 60 °C for 48 h. Work-up was carried out as in the preparation of (**8**) above, except that the eluting solvent in the chromatography was light petroleum–ethyl acetate (55:45), to yield the *title compound* (**12**) (440 mg, 60.1%) as an oil with i.r. and n.m.r. spectra corresponding to those previously reported.[19]

Ethyl 1-(3,4-*Dimethoxyphenyl*)-4-*oxocyclohex*-2-*enecarboxylate* (**13**).—The mixture of keto esters, (**10a**) and (**10b**), (2.02 g, 12.0 mmol) was added dropwise with stirring to a solution of 3,4-dimethoxyphenyl-lead triacetate (**6**) (12.54 g, 24.0 mmol) in dimethyl sulphoxide (20 ml), and the mixture was stirred at 40 °C for 48 h. The work-up and chromatography was carried out as in the preparation of (**12**) above, to afford the *title compound* (**13**) (1.92 g, 52.5%) as an oil (Found: C, 66.7; H, 6.8. $C_{17}H_{20}O_5$ requires C, 67.1; H, 6.6%); $\nu_{max.}$(film) 1 725, 1 680, and 1 510 cm^{-1}; $\lambda_{max.}$(EtOH) 230 and 281 nm (ε 16 600 and 4 570); $\delta_H(CDCl_3)$ 1.23 (3 H, t, *J* 7.0 Hz, Me), 2.1—2.9 (4 H, m, 2 × CH_2), 3.86 (6 H, s, 2 × OMe), 4.22 (2 H, q, *J* 7.0 Hz, CH_2), 6.21 (1 H, d, *J* 10.0 Hz, 3-H), 6.70—6.90 (3 H, m, ArH), and 7.35 (1 H, d, *J* 10.0 Hz, 2-H); *m*/*z* 304 (*M*, 20%) and 231 (*M* − CO_2Et, 100).

Reaction of Ethyl 3-*Ethyl*-2-*methyl*-4-*oxocyclohex*-2-*enecarboxylate* (**14**) *with* p-*Methoxyphenyl-lead Triacetate* (**2**).—*p*-Methoxyphenyl-lead triacetate (2.95 g, 6.0 mmol) was added with stirring to a solution of the keto ester (**14**) (0.63 g, 3.0 mmol) and DMAP (1.10 g, 9.0 mmol) in chloroform (5 ml), and the mixture was stirred at 60 °C for 48 h. The reaction was worked up as for the preparation (**8**) above, and the crude product was fractionated by p.l.c. in light petroleum–ether (1:1). Two major products were isolated and these were purified by h.p.l.c. using light petroleum–ethyl acetate (91:9) as the eluting solvent. The less polar material, *ethyl* 3-*ethyl*-1-(p-*methoxyphenyl*)-2-*methyl*-4-*oxocyclohex*-2-*enecarboxylate* (**15**) (27.2 mg, 2.9%), was obtained as an oil (Found: M^+, 316.1655. $C_{19}H_{24}O_4$ requires M^+, 316.1674); $\nu_{max.}$($CHCl_3$) 1 725 and 1 665 cm^{-1}; $\lambda_{max.}$(EtOH) 228 and 244 nm (ε 16 220 and 14 450); $\delta_H(CDCl_3)$ 1.02 (3 H, t, *J* 7.0 Hz, Me), 1.30 (3 H, t, *J* 7.0 Hz, Me), 1.85 (3 H, s, 2-Me), 2.10—2.90 (6 H, m, 3 × CH_2), 3.80 (3 H, s, OMe), 4.29 (2 H, q, *J* 7.0 Hz, CH_2), 6.88 and 7.08 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H and 6′-H respectively); *m*/*z* 316 (*M*, 23%) and 243 (*M* − CO_2Et, 100).

The more polar material was *ethyl* 3-*ethyl*-3-(p-*methoxyphenyl*)-2-*methyl*-4-*oxocyclohexa*-1,5-*dienecarboxylate* (**18**) (47.1 mg, 5.0%), obtained as an oil (Found: M^+, 314.1498. $C_{19}H_{22}O_4$ requires M^+, 314.1518); $\nu_{max.}$(film) 1 720 and 1 660 cm^{-1}; $\lambda_{max.}$(EtOH) 229, 275, 283, and 309 nm (ε 11 480, 3 715, 3 548, and 3 390); $\delta_H(CDCl_3)$ 0.76 (3 H, t, *J* 7.0 Hz, Me) 1.39 (3 H, t, *J* 7.0 Hz, Me), 2.06 (3 H, s, 2-Me), 2.08—2.78 (2 H, m, CH_2), 3.76 (3 H, s, OMe), 4.34 (2 H, q, *J* 7.0 Hz, CH_2), 6.06 (1 H, d, *J* 10.1 Hz, 5-H), 6.83 and 7.09 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H and 6′-H respectively), and 7.61 (1 H, d, *J* 10.1 Hz, 6-H).

Reaction of Ethyl 3-*Methyl*-4-*oxocyclohex*-2-*enecarboxylate* (**16**) *with* p-*Methoxyphenyl-lead Triacetate* (**2**).—*p*-Methoxyphenyl-lead triacetate (1.47 g, 3.0 mmol) was added to a solution of keto ester (**16**) (0.27 g, 1.5 mmol) in chloroform (2.5 ml) containing pyridine (0.35 g, 4.5 mmol), and the mixture was heated and stirred at 60 °C for 48 h. The reaction was worked up as in the preparation of (**8**) above, and the crude product was separated into two fractions by p.l.c. using light petroleum–ether (1:1). Both fractions were further purified by h.p.l.c. with light petroleum–ethyl acetate (88:12) as the eluting solvent. The less polar material, *ethyl* 1-(p-*methoxyphenyl*)-3-*methyl*-4-*oxocyclohex*-2-*enecarboxylate* (**17**) (11.2 mg, 2.5%), was obtained as an oil (Found: M^+, 288.1352. $C_{17}H_{20}O_4$ requires 288.1361); $\nu_{max.}$(film) 1 725, 1 700sh, and 1 620 cm^{-1}; $\lambda_{max.}$(EtOH) 235, 282, and 289 nm (ε 10 720, 1 450, and 1 480); $\delta_H(CDCl_3)$ 1.23 (3 H, t, *J* 7.1 Hz, Me), 2.08 (3 H, d, *J* 1.5 Hz, 3-Me), 2.28—2.40 (2 H, m, 2 × 6-H), 2.48—2.74 (2 H, m, 2 × 5-H), 3.81 (3 H, s, OMe), 4.20 (2 H, q, *J* 7.1 Hz, CH_2), 6.88 and 7.22 (4 H, AA′BB′, 3′-H and 5′-H and 2′-H and 6′-H respectively), and 7.11 (1 H, q, *J* 1.5 Hz, 2-H); $\delta_C(CDCl_3)$ 13.96 (q, Me), 16.23 (q, Me), 33.96 (t, CH_2), 34.61 (t, CH_2), 52.07 (s, C-1), 55.19 (q, OMe), 61.82 (t, OCH_2), 114.08 (d, C-3′ and C-5′), 127.39 (d, C-2′ and C-6′), 129.70 (s, C-1′), 132.91 (s, C-4′, 136.29 (s, C-3), 145.12 (d, C-2), 172.71 (s, CO_2), and 198.62 (s, C-4); *m*/*z* 288 (*M*, 25%) and 215 (*M* − CO_2Et, 100).

The more polar material, *ethyl* 3,5,5-*tris*(p-*methoxyphenyl*)-3-*methyl*-4-*oxocyclohex*-1-*enecarboxylate* (**19**) (66.8 mg, 9.1%), was obtained as a colourless oil (Found: M^+, 500.2206. $C_{31}H_{32}O_6$ requires M^+, 500.2200); $\nu_{max.}$(film) 1 710 and 1 500 cm^{-1}; $\lambda_{max.}$(EtOH) 224 and 274 nm (ε 25 700 and 5 130); $\delta_H(CDCl_3)$ 1.35 (3 H, t, *J* 7.1 Hz, Me), 1.55 (3 H, s, 3-Me), 3.24 (1 H, dd, J_{gem} 17.7 Hz, $J_{2,6}$ 3.0 Hz, 6_{ax}-H), 3.63 (1 H, d, J_{gem} 17.7 Hz, 6_{eq}-H), 3.72 (3 H, s, OMe), 3.74 (3 H, s, OMe), 3.76 (3 H, s, OMe), 4.31 (2 H, q, *J* 7.1 Hz, CH_2), 6.58—7.00 (12 H, m, 3 × AA′BB′ spin systems), and 6.97 (1 H, d, $J_{2,6}$ 3.0 Hz, 2-H); *m*/*z* 500 (*M*, 41%), 472 (*M* − CO, 94), 254 (Ar_2C_2O, 83), and 227 (Ar_2CH, 100).

Reaction of the Mixture of Isomeric Keto Esters (**20a**) *and* (**20b**) *with* p-*Methoxyphenyl-lead Triacetate* (**2**).—*p*-Methoxyphenyl-lead triacetate (2.95 g, 6.0 mmol) was added to a solution of the mixture of keto esters (**20a**) and (**20b**) (0.589 g, 3.0 mmol) in chloroform (5 ml) containing DMAP (1.10 g, 9.0 mmol), and the mixture was stirred at 60 °C for 48 h. The reaction was worked up as in the preparation of (**8**) above, and the crude product was separated by p.l.c. into three fractions. These were then purified by h.p.l.c. using light petroleum–ethyl acetate (9:1) as the eluting solvent.

The least polar compound, *ethyl* 2,6-*dimethyl*-1-p-*methoxyphenyl*)-4-*oxocyclohex*-2-*enecarboxylate* (**21**) (78 mg, 8.6%), was obtained as an oil (Found: M^+, 302.1524. $C_{18}H_{22}O_4$ requires M^+, 302.1518); $\nu_{max.}$($CHCl_3$) 1 725 and 1 660 cm^{-1}; $\lambda_{max.}$(EtOH) 228 and 275 nm (ε 20 890 and 2 630); δ_H 1.00 (3 H, d, *J* 6.0 Hz, 6-Me), 1.30 (3 H, t, *J* 7.0 Hz, Me), 1.81 (3 H, d, *J* 1.3 Hz, 2-Me), 2.40 (1 H, m, 6-H), 2.53—2.70 (2 H, m, 2 × 5-H), 3.82 (3 H, s, OMe), 4.29 (2 H, q, *J* 7.0 Hz, CH_2), 6.12 (1 H, q, *J* 1.3 Hz, 3-H), and 6.91 and 7.20 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H and 6′-H respectively); *m/z* 302 (*M*, 50%) and 229 (*M* − CO_2Et, 100).

The fraction of intermediate polarity yielded *ethyl* trans-2,6-*dimethyl*-3-(p-*methoxyphenyl*)-4-*oxocyclohex*-2-*enecarboxylate* (**22**) (11.5 mg, 1.3%) as a crystalline solid, m.p. 71—74 °C (Found: M^+, 302.1520. $C_{18}H_{22}O_4$ requires M^+, 302.1518); $\nu_{max.}$($CHCl_3$) 1 725, 1 660, and 1 605 cm^{-1}; $\lambda_{max.}$(EtOH) 228 and 276 nm (ε 19 500 and 3 720); δ_H($CDCl_3$) 1.15 (3 H, d, *J* 6.5 Hz, 6-Me), 1.32 (3 H, t, *J* 7.0 Hz, Me), 1.80 (3 H, d, *J* 0.8 Hz, 2-Me), 2.20—2.85 (3 H, m, 2 × 5-H and 6-H), 3.19 (1 H, dq, $J_{1,6}$ 8 Hz, 1-H), 3.81 (3 H, s, OMe), 4.26 (2 H, q, *J* 7.0 Hz, CH_2), and 6.92 and 6.97 (4 H, AA′BB′, 3′-H and 5′-H, 2′-H and 6′-H respectively); *m/z* 302 (*M*, 100%), 229 (*M* − CO_2Et, 73), and 201 (229 − CO, 54).

The most polar compound, *ethyl* 2,6-*dimethyl*-1,3-*bis*-(p-*methoxyphenyl*)-4-*oxocyclohex*-2-*enecarboxylate* (**23**) (11.8 mg, 1.0%) was obtained as a crystalline solid, m.p. 109—112 °C (Found: M^+, 408.1939. $C_{25}H_{28}O_5$ requires M^+, 408.1936); $\nu_{max.}$($CDCl_3$) 1 725, 1 665, and 1 610 cm^{-1}; $\lambda_{max.}$(EtOH) 228 and 275 nm (ε 41 690 and 8 320); δ_H($CDCl_3$) 1.03 (3 H, d, *J* 6.5 Hz, 6-Me); 1.33 (3 H, t, *J* 7.0 Hz, Me), 1.57 (3 H, s, 2-Me), 2.50—2.80 (3 H, m, 2 × 5-H and 6-H), 3.818 (3 H, s, OMe), 3.822 (3 H, s, OMe), 4.51 (2 H, q, *J* 7.0 Hz, CH_2), 6.92 and 7.02 (4 H, AA′BB′), and 6.92 and 7.30 (4 H, AA′BB′).

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