Reductive Cleavage of Arylcyclopropyl Ketones[1]

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Arylcyclopropyl aryl ketones undergo clean but slow reductive cleavage to 4-arylbutyrophenones when heated with zinc in ethanol. Replacement of one of the aryl groups by an alkyl group strongly inhibits reaction. This effect is in part overcome by the use of a higher boiling alcohol. When substituted at the cyclopropyl methylene position by an ethoxycarbonyl group these cyclopropyl ketones also undergo cleavage but with the unexpected formation of the ethyl 3,5-diaryl-5-oxopentanoates (**22**). In general, the results are consistent with the formation of an anion-radical intermediate.

Following the successful selective conversion of arylcyclopropyl ketones into a variety of classes of functionalised compounds,[2] we sought new synthetic applications for these substrates. Reductive opening of cyclopropyl ketones appeared to be attractive, since reaction would provide not only a simple homologative method to a wide variety of long-chain aromatic ketones but also a convenient new entry to open-chain lignan lactones[3] and bisbenzocyclo-octadiene lignans.[4]

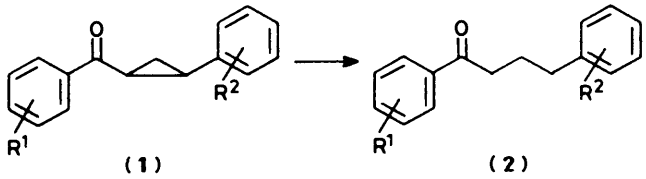
A variety of methods[1,5] exists for the reductive cleavage of cyclopropyl ketones. Whereas hydrogenolysis is strongly affected by steric factors,[5] lithium in liquid ammonia results in the rupture of that bond which overlaps most efficiently with the π orbital of the carbonyl group.[5] Chromium(II)-induced cleavage is subject to subtle stereoelectronic effects.[5] The mild procedure involving zinc and zinc chloride reported by Dekker[6] and shown to be an efficient method for the reductive cleavage of strained-ring 1,2-dicarbonyl compounds was selected for investigation. From our preliminary results,[1] it appears that the ease of cleavage depends on the ability of substituents to stabilise a radical-anion intermediate.

The cyclopropyl ketone (**1b**) was studied initially. When ketone (**1b**) was treated with excess of zinc and zinc chloride in boiling ethanol for 10 min (Dekker's conditions[6]) no reaction was observed. However, when the period of heating was extended to 30 h a high yield of compound (**2b**) exclusively was obtained. None of the reactant (**1b**) was detected. The structure of compound (**2b**) was confirmed by its reduction to the alcohol (**3**) which was identical with an authentic sample.[7]

Since the previous synthesis[7] of alcohol (**3**) had involved six steps and had proceeded in low overall yield, and since the present method afforded alcohol (**3**) in 77% overall yield in three operationally simple reactions from the corresponding chalcone, it was decided to examine the scope and limitations of the method.

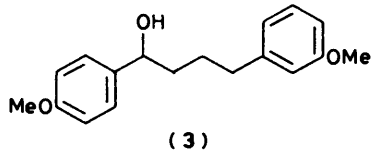
A wide range of cyclopropyl ketones was investigated. The results are outlined in Table 1. The reaction worked well with the cyclopropyl ketones of general type (**1**) (see entries 1—8, Table 1). The cyclopropyl ketones (**4**), (**6**), and (**8**) were also found to react although at a much slower rate to give high yields of the aromatic ketones as the only product. None of the corresponding alcohols such as (**3**) was formed. Since the cyclopropyl ketones are easily prepared in one step from the corresponding chalcone, enone, or dieneone, these results constitute a short, practical, and high-yield route to a variety of aromatic ketones.

Subsequently, we found that zinc chloride was not necessary for the reaction (see entries 2, 4, 6, and 8, Table 1). In addition, the substituent groups on the aromatic rings had no apparent effect on the relative rates of the reaction. For instance, ketones (**1a**) and (**1c**) showed a similar starting material-to-product



(**1**) (**2**)

	R^1	R^2
a;	H	H
b;	4-OMe	3-OMe
c;	3-OMe	4-OMe
d;	3,4-$(OMe)_2$	3,4-$(OMe)_2$



(**3**)

ratio when the reaction was stopped before completion (entries 5 and 7, Table 1). The efficiency of the reaction was highly solvent dependent. Thus, when compound (**1b**) was treated with zinc (or zinc and zinc chloride) in refluxing benzene or toluene no reaction was observed and starting material (**1b**) was recovered unchanged. Use of zinc amalgam[8] did not affect the rate of the reaction. Attempts to separate the partially cleaved compound (**10**) from the crude mixture of the starting material (**4a**) and final product (**5a**) (see entry 11, Table 1) failed. However, the structure of compound (**10**) was deduced from a comparison of the ^{13}C n.m.r. spectrum of the crude mixture with those of compounds (**4a**) and (**5a**). This was also supported by the exclusive conversion into the ketone (**5a**) upon prolonged treatment of the crude mixture under standard conditions. The structure of compound (**11**) was similarly assigned. It appeared, therefore, that the reductive cleavage of the biscyclopropyl ketones (**4a**) and (**6**) involved stepwise cleavage of the cyclopropane rings rather than simultaneous openings of both cyclopropane rings. However, no attempt was made to convert compounds (**4a**) and (**6**) selectively into (**10**) and (**11**), respectively.

Attempted reductive cleavage of the cyclopropyl ketones (**12a**) and (**12b**) to the ketones (**13a**) and (**13b**), respectively, under standard conditions failed, even when prolonged reaction periods (8 days) were employed.[9] The starting materials (**12a**) and (**12b**) were recovered quantitatively.

Alkyl carbonyl derivatives (**14**) were quite resistant to

Table 1. Reductive cleavage of cyclopropyl ketones[a]

Entry	Reactant	Method	Time (h)	Product [yield (%)][b]
1	(**1b**)	A[c]	30	(**2b**) [90]
2	(**1b**)	B[d]	30	(**2b**) [91]
3	(**1a**)	A	30	(**2a**) [90]
4	(**1a**)	B	30	(**2a**) [90]
5	(**1a**)	A	15	(**1a**):(**2a**) = 1:1[e]
6	(**1c**)	B	30	(**2c**) [90]
7	(**1c**)	A	15	(**1c**):(**2c**) = 1:1[e]
8	(**1d**)	B	30	(**2d**) [89]
9	(**4a**)	C[f]	288	(**5a**) [85]
10	(**4a**)	D[g]	288	(**5a**) [80]
11	(**4a**)	C	144	(**4a**) + (**5a**) + (**10**)[h]
12	(**4b**)	C	288	(**5b**) [90]
13	(**6**)	C	288	(**7**) [80]
14	(**6**)	D	288	(**7**) [81]
15	(**6**)	C	144	(**6**) + (**7**) + (**11**)[h]
16	(**8**)	A	120	(**9**) [88]
17	(**14a**)	B	432	(**14a**):(**15a**) = 30:70[e]
18	(**14a**)	E[i]	288	(**15a**) [80]
19	(**16**)	E	264	(**17**) [89]

[a] All reactions were carried out under nitrogen. A *ca.* 0.05M solution of the reactant in the indicated solvent was treated with the indicated reagent and was stirred and heated at reflux for the period indicated. [b] All yields, unless otherwise stated, refer to isolated pure products. [c] Method A: Zn (3 equiv.), $ZnCl_2$ (3 equiv.), refluxing EtOH. [d] Method B: Zn (3 (equiv.), only, refluxing EtOH. [e] Products were not isolated; ratio was determined by ^1H n.m.r. spectroscopy. [f] Method C: Zn (5 equiv.), $ZnCl_2$ (5 equiv.), refluxing EtOH. [g] Method D: Zn (5 equiv.), only, refluxing EtOH. [h] Products were not isolated; determined by ^{13}C n.m.r. spectroscopy. [i] Method E: Zn (5 equiv.), $ZnCl_2$ (5 equiv.), refluxing butan-1-ol

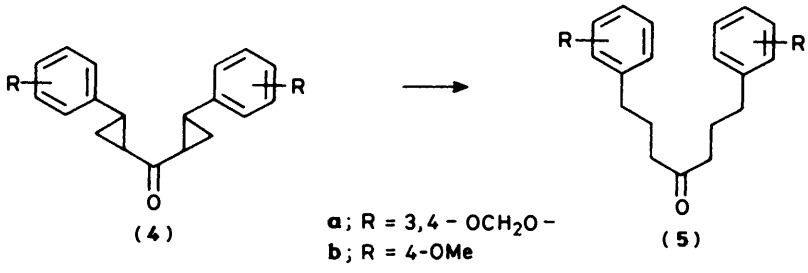
reductive opening. The ketone (**14a**) required 18 d at reflux temperature. The ketone (**14b**) was of comparable reactivity. No attempt was made to isolate (**15b**). This inconvenience was partly circumvented by employing butan-1-ol (entry 18, Table 1). The ketone (**16**) was readily converted into compound (**17**) in 89% isolated yield under these conditions.

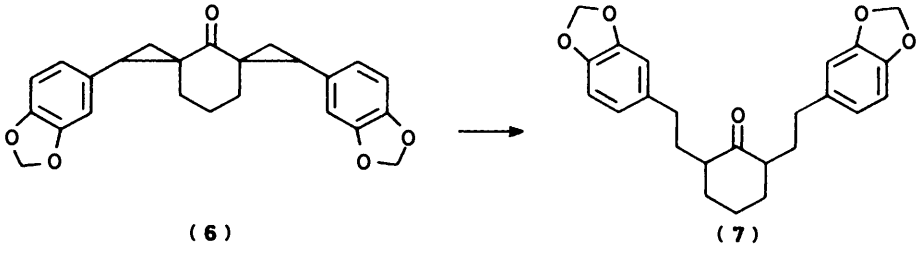
The rigid cyclopropyl ketone (**18**) was next investigated. Attempted reductive cleavage of this compound failed, with none of the expected product (**19**) being formed. This reluctance of compound (**18**) to undergo cleavage was probably due to a combination of steric and stereoelectronic effects.[2b,5,10]

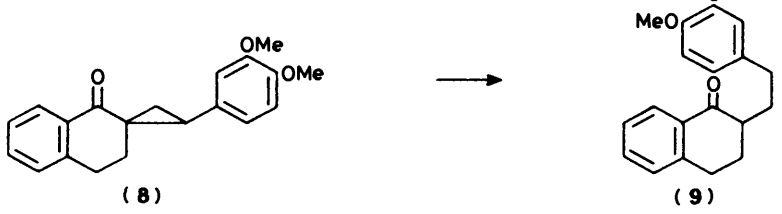
Since the keto esters (**21**) are key intermediates[11] in the synthesis of a wide range of naturally occurring lignans,[3b] we next examined the reductive cleavage of the keto esters (**20a**—**e**). In a preliminary investigation we found that the cyclopropyl ester (**23**) was recovered unchanged using methods C—E (see Table 1). This result suggested that at least bond c in keto esters (**20**) would not cleave under these reaction conditions.

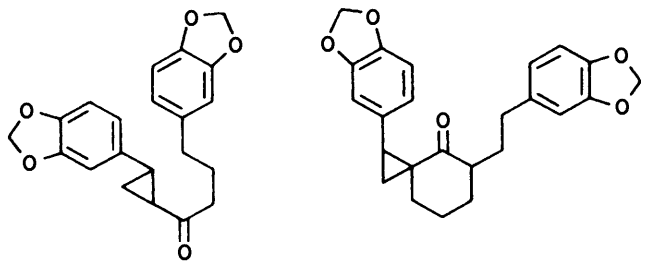
In the event, when keto ester (**20a**) was treated with zinc and zinc chloride according to method C for 30 h, the δ-keto ester (**22a**) was obtained in 85% yield as the only product. Spectral data were used to differentiate between isomers (**21a**) and (**22a**). The identity of compound (**22a**) was unequivocally confirmed by comparison with a sample prepared *via* conjugate addition of diethyl malonate to chalcone.[12]

Cleavage of bond a in keto esters (**20b**—**e**) also occurred exclusively. The results are presented in Table 2. None of the desired products (**21a**—**e**) was observed. However, the features which are noteworthy include: (a) excellent yields of products; (b) simple procedures, and (c) no side-products. Thus, the reaction appears to offer a synthetically useful method for the preparation of a variety of substituted aromatic keto esters of general type (**22**) which have potential as synthetic inter-

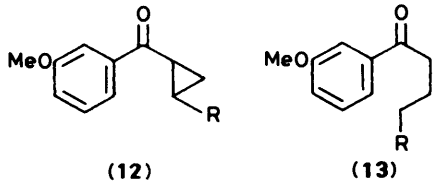






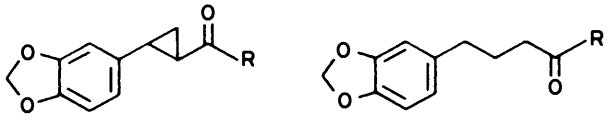


(10) (11)



(12) (13)

a; R = Bu^t
b; R = H



(14) (15)

a; R = Et
b; R = Bu^t

Table 2. Reductive cleavage of cyclopropyl keto esters[a]

Entry	Reactant	Zn (equiv.)	$ZnCl_2$ (equiv.)	Time (h)	Product [Yield (%)][b]
1	(**20a**)	5	5	72	(**22a**) [80]
2	(**20b**)	5	5	72	(**22b**) [85]
3	(**20c**)	5	5	72	(**22c**) [81]
4	(**20c**)	10	5	30	(**22c**) [88]
5	(**20c**)	30	15	18	(**22c**) [86]
6	(**20d**)	3	3	96	(**22d**) [80]
7	(**20d**)	15	6	72	(**22d**) [85]
8	(**20e**)	5	5	72	(**22e**) [75]
9	(**20e**)	10	5	50	(**22e**) [73]
10	(**20d**)	3		100	

[a] All reactions were carried out under nitrogen. A *ca.* 0.05M solution of the reactant in absolute EtOH was treated with the indicated reagent and the reaction mixture was heated at reflux for the period indicated. [b] Isolated pure product.

mediates in the synthesis of the novel lignans sugiresinol (**24**)[13] and sequirin-B (**25**).[14]

The rate of reaction was found to increase in proportion to the amount of the reagent (compare, for example, entries 3, 4, and 5, Table 2). However, use of a very large excess of reagents, particularly zinc, was undesirable since it absorbed the product and caused some difficulties during work-up. As a result, use of 5 equiv. each of zinc and zinc chloride was considered to be optimum.

Zinc chloride was necessary for the reductive opening of cyclopropyl keto esters. Thus, prolonged heating of compound (**20d**) with zinc in ethanol gave no ring-opening product (**22d**) whatsoever, while in the presence of zinc chloride it was readily converted into the product (compare entries 6 and 10, Table 2). In contrast, the cyclopropyl ketone (**1d**) was easily cleaved in the absence of zinc chloride to form compound (**2d**) (entry 8, Table 1). Formally, cleavage of bond a was slower than that of bond b (compare, for example, entry 8, Table 1 with entry 7, Table 2). The presence of the ethoxycarbonyl group strongly inhibited cleavage of bond b whereas zinc chloride catalysed cleavage of bond a. It seems probable that a species such as (**26**) was involved. Such co-ordination would probably weaken bond a and facilitate its reductive cleavage. It is not clear, however, why such an arrangement would inhibit cleavage of bond b.

The effect of substituents and solvent, and the imperceptible effect of aryl substituents on the rate of this dissolving metal reduction, are consistent with the mechanism involving species (**27**)—(**30**). Thus formation of the intermediate (**28**) and hence the overall rate should be facilitated by the presence of an aryl (Ar) *vis-à-vis* an alkyl (R) group.[10,15] This was observed (compare, for example, entries 9 and 18 with 8, Table 1). Similarly, the rate should be enhanced by the presence of an aryl (Ar^1) *via-à-vis* an alkyl (R^1) group which would facilitate the formation of intermediate (**29**).[10,15] This effect was also observed (compare entry 19 with entry 7, Table 1). Further circumstantial evidence for this mechanism was provided by application of these reagents and conditions to the chalcone (**31**). The dimer (**33**) was formed in addition to the dihydrochalcone (**32**). This strongly indicated the involvement of an anion-radical intermediate analogous to the postulated intermediate (**29**).

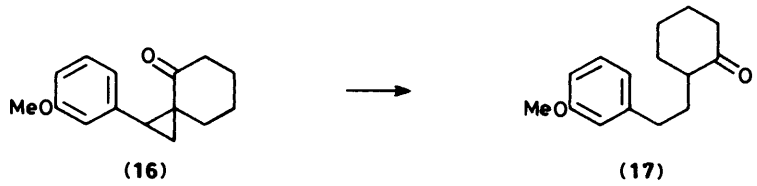
Experimental

^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R20A spectrometer at 60 MHz for $CDCl_3$ solutions. ^{13}C N.m.r. spectra were recorded on a JEOL FX60 spectrometer for $CDCl_3$ solutions unless otherwise stated.

The synthesis of the cyclopropyl ketones (**1a**—**d**),[2b] (**4b**),[16] (**12a**),[2b] (**12b**),[2b] (**18**),[2b] the cyclopropyl keto esters (**20a**—**e**),[17] the carbinol (**3**),[7] and the chalcone (**31**)[18] have been described previously. The cyclopropane (**23**)[19] was prepared according to the literature method. Mixtures of diastereoisomers were used throughout. Light petroleum refers to the fraction boiling in the range 40—60 °C.

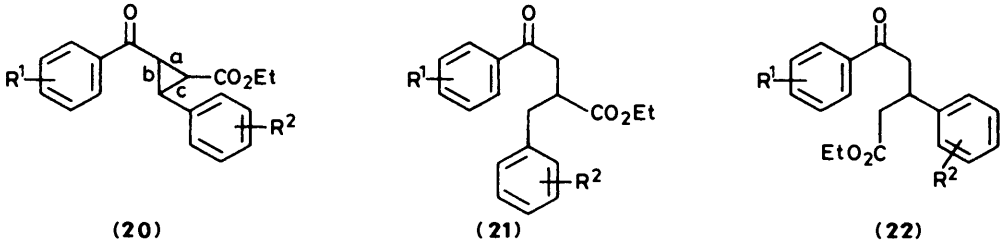
The Biscyclopropyl Ketone (**4a**).—Treatment of (*E,E*)-1,5-bis-(3,4-methylenedioxyphenyl)penta-1,4-dien-3-one[20] (600 mg, 186 mmol) in dimethyl sulphoxide (DMSO, 10 ml) with dimethyloxosulphonium methylide (10 ml), prepared from trimethyloxosulphonium iodide (892 mg, 4.1 mmol) and sodium hydride (80%; 123 mg, 4.1 mmol) in DMSO (10 ml), at room temperature for 2 h followed by the usual[16] work-up gave the *cyclopropyl ketone* (**4a**) as an oil after preparative t.l.c. (p.l.c.) [ether–light petroleum (7:3)] (600 mg, 95%) (Found: C, 72.0; H, 5.3. $C_{21}H_{18}O_5$ requires C, 72.0; H, 5.1%); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 1.29 (2 H, m), 1.70 (2 H, m), 2.3 (4 H, m), 5.96 (4 H, s, 2 × OCH_2O), and 6.71 (6 H, m, ArH); δ_C 19.10, 28.98, 29.17, 33.01, 100.97, 106.43, 108.12, 119.55, 134.17, 146.26, 147.81, and 206.74.

The Biscyclopropyl Ketone (**6**).—Similar treatment of 2,6-bis-(3,4-methylenedioxybenzylidene)cyclohexan-1-one[18] (1 g, 2.76 mmol) in DMSO (16 ml) with the methylide, prepared from trimethyloxosulphonium iodide (1.33 g, 6.1 mmol) and sodium hydride (80%; 183 mg, 6.1 mmol) in DMSO (10 ml), at room temperature for 4 h, followed by p.l.c. [ether–light petroleum (7:3)] gave the *ketone* (**6**) as an oil (696 mg, 80%) (Found: C, 73.2; H, 5.3. $C_{24}H_{22}O_5$ requires C, 73.8; H, 5.6%); $\nu_{max.}$ 1 665 and 1 610 cm^{-1}; δ_H 0.91—2.11 (10 H, m), 2.81 (2 H, m), 6.01 (4



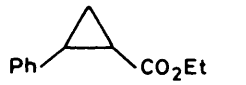
(16) (17)

(18) (19)



(20) (21) (22)

	R^1	R^2
a;	H	H
b;	3-OMe	4-OMe
c;	3,4-OCH_2O-	3,4-OCH_2O-
d;	3,4-$(OMe)_2$	3,4-$(OMe)_2$
e;	3 4-OCH_2O-	3,4,5-$(OMe)_3$



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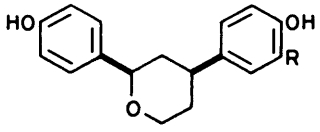
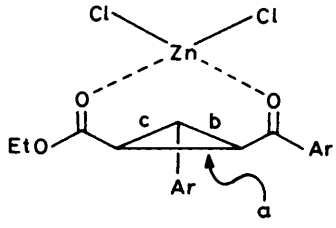


(24) R = H
(25) R = OH



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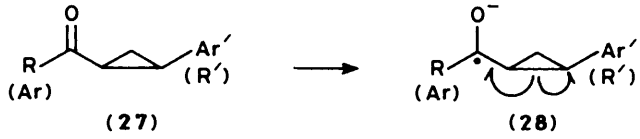

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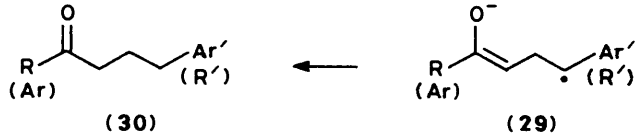
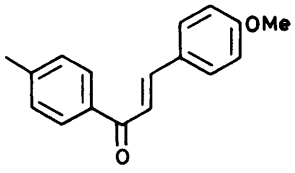


(30) (29)

H, s, 2 × OCH_2O), and 6.71 (6 H, br s, ArH); δ_C 21.64, 22.61, 23.60, 28.20, 28.59, 34.76, 35.22, 36.84, 100.97, 107.99, 109.61, 122.41, 130.86, 146.45, 147.55, and 210.78.

The Cyclopropyl Ketone (**8**).—Similar treatment of 2-(3,4-dimethoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[18] (500 mg, 1.7 mmol) in DMSO (10 ml) with the methylide, prepared from trimethyloxosulphonium iodide (445 mg, 2 mmol) and sodium hydride (80%; 60 mg, 2 mmol) in DMSO (6 ml), at room temperature for 35 min, followed by p.l.c. of the crude oil [ether–light petroleum (1:1)] gave the *ketone* (**8**) as an oil (418 mg, 80%) (Found: 77.6; H, 6.3. $C_{20}H_{20}O_3$ requires C, 77.9; H, 6.5%); $\nu_{max.}$ 1 660 and 1 600 cm^{-1}; δ_H 1.22 (1 H, m), 1.75 (3 H, m), 2.75 (3 H, m), 3.82 (6 H, s, 2 × OMe), 6.75 (3 H, s, ArH), and 6.90—8.11 (4 H, m, ArH).

The Cyclopropyl Ketone (**14a**).—To a solution of the methylide, prepared from trimethyloxosulphonium iodide (534 mg, 2.45 mmol) and sodium hydride (80%; 74 mg, 2.45 mmol) in DMSO (7 ml), was added a solution of 1-(3,4-methylenedioxyphenyl)pent-1-en-3-one[18] (500 mg, 2.45 mmol) in DMSO (8 ml) at 20 °C. After being stirred at 20 °C for 50 min, the solution was poured onto water and extracted with chloroform. P.l.c. [ether–light petroleum (7:3)] of the crude oil gave the *cyclopropyl ketone* (**14a**) as an oil (250 mg, 47%) (Found: C, 71.0; H, 6.2. $C_{13}H_{14}O_3$ requires C, 71.6; H, 6.4%); $\nu_{max.}$ 1 680 and



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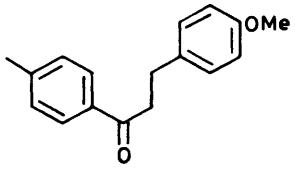

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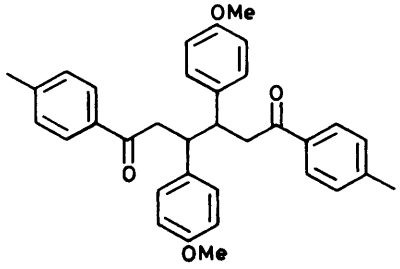

(33)

1 600 cm^{-1}; δ_H 1.10 (3 H, t, *J* 7.5 Hz, Me), 1.2—2.41 (4 H, m), 2.49 (2 H, q, *J* 7.5 Hz, CH_2CO), 5.88 (2 H, s, OCH_2O), and 6.41—7.21 (3 H, m, ArH).

The Cyclopropyl Ketone (**14b**).—Similar treatment of a solution of 1-(3,4-methylenedioxyphenyl)-4,4-dimethylpent-1-en-3-one[21] (1.7 g, 7.32 mmol) in DMSO (20 ml) with the methylide, prepared from trimethyloxosulphonium iodide (1.75 g, 8.0 mmol) and sodium hydride (80%; 243 mg, 8.0 mmol) in DMSO (20 ml), at room temperature for 1.5 h followed by the usual work-up gave an oil, which after short column chromatography (SiO_2) [ether–light petroleum (2:3)] afforded the cyclopropyl ketone (**14b**) (1.51 g, 85%) as an almost colourless oil; $\nu_{max.}$ 1 670 cm^{-1}; δ_H 1.20 (9 H, s, 3 × Me), 1.21—1.70 (2 H, m), 2.31 (2 H, m), 5.91 (2 H, s, OCH_2O), and 6.61 (3 H, m, ArH); δ_C 17.93, 26.12, 27.55, 29.04, 43.79, 100.97, 106.69, 108.19, 119.68, 134.37, 146.32, 147.88, and 212.78.

The Cyclopropyl Ketone (**16**).—To a solution of the methylide, prepared from trimethyloxosulphonium methylide (436 mg, 1.9 mmol) and sodium hydride (80%; 60 mg, 1.9 mmol) in DMSO (5 ml), was added a solution of 2-(3-methoxybenzylidene)cyclohexan-1-one[22] (360 mg, 1.7 mmol) in DMSO (8 ml) at room temperature. After being stirred for 2 h at room temperature, the solution was poured into water, acidified (5% HCl), and extracted with chloroform. P.l.c. [ether–light petroleum (3:7)] gave the *cyclopropyl ketone* (**16**) as an oil (196 mg, 51%) (Found: C, 78.0; H, 7.3. $C_{15}H_{18}O_2$ requires C, 78.3; H, 7.8%); $\nu_{max.}$ 1 675 and 1 600 cm^{-1}; δ_H 0.81—3.0 (11 H, m), 3.78 (3 H, s, OMe), and 6.41—7.50 (4 H, m, ArH); δ_C 19.62, 23.20, 24.11, 28.07, 34.18, 35.22, 39.89, 55.01, 111.89, 115.12, 121.56, 129.10, 138.33, 159.51, and 210.64.

General Procedure for Reductive Cleavage of Cyclopropyl Ketones (*see also Table* 1).—A solution of the cyclopropyl ketone (1 mmol) in the indicated solvent (5—6 ml) was treated with the indicated reagent at room temperature. The reaction mixture was then heated at reflux under nitrogen for the time indicated. The cooled mixture was diluted with chloroform, filtered, and the solvent was removed under reduced pressure. The residue was dissolved in chloroform, washed successively with dil. hydrochloric acid (5%) and brine, and dried (sodium sulphate). Removal of the solvent gave the crude product which was analysed by n.m.r. spectroscopy before being purified by p.l.c. [ether–light petroleum (2:3)] to give the pure product.

The ketone (**2a**). $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ 2.12 (2 H, q, *J* 8 Hz, CH_2), 2.75 (4 H, pentet, *J* 8 Hz, $COCH_2$ and $ArCH_2$), 3.82 and 3.90 (6 H, 2 × s, 2 × OMe), 6.61—7.40 (6 H, m, ArH), and 7.90 (2 H, d, of AB, *J* 9 Hz, ArH).

Reduction of ketone (**2a**) (200 mg) with lithium aluminium hydride (120 mg) in ether (8 ml) at room temperature for 3 h gave the alcohol (**3**) (161 mg, 80%), identical (i.r., n.m.r., and t.l.c.) with an authentic sample prepared by a different route.[7]

The ketone (**2b**). M.p. 45—47 °C (Found: C, 85.2; H, 7.0. $C_{16}H_{16}O$ requires, C, 85.7; H, 7.1%); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 2.12 (2 H, q, *J* 7.5 Hz, CH_2), 2.81 (4 H, pentet, *J* 7.5 Hz, $COCH_2$ and $ArCH_2$), and 7.21—8.11 (10 H, m, ArH).

The ketone (**2c**). (Found: C, 76.2; H, 7.1. $C_{18}H_{20}O_3$ requires C, 76.1; H, 7.0%) $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 2.08 (2 H, q, *J* 7.5 Hz, CH_2), 2.78 (4 H, pentet, *J* 7.5 Hz, $COCH_2$ and $ArCH_2$), 3.82 and 3.90 (6 H, 2 × s, 2 × OMe), and 6.71—7.70 (8 H, m, ArH).

The ketone (**2d**). (Found: C, 70.0; H, 6.9. $C_{20}H_{24}O_5$ requires C, 69.8; H, 7.0%); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 2.02 (2 H, q, *J* 7.5 Hz, CH_2), 2.63 (4 H, pentet, *J* 7.5 Hz, $COCH_2$ and $ArCH_2$), 2.79 and 2.88 (12 H, 2 × s, 4 × OMe) and 6.66—7.62 (6 H, m, ArH).

The ketone (**5a**). (Found: C, 71.0; H, 6.1. $C_{21}H_{22}O_5$ requires C, 71.2; H, 6.2%); $\nu_{max.}$ 1 710 and 1 605 cm^{-1}; δ_H 1.75 (4 H, br q, *J* 7 Hz, 2 × CH_2), 2.29 (8 H, p, *J* 7 Hz, 2 × $ArCH_2$ and 2 × $COCH_2$), 5.88 (4 H, s, 2 × OCH_2O) and 6.62 (6 H, br s, ArH); δ_C 25.40, 34.76, 41.78, 100.77, 108.12, 108.83, 121.17, 135.41, 145.73, 147.62, and 210.44.

When the reaction was stopped before completion (see entry 11, Table 1), a mixture of ketones (**4**), (**5a**), and (**10**) was obtained as was evident by the ^{13}C n.m.r. spectrum of the crude mixture: δ_C 18.58, 19.10, 24.88, 25.40, 28.78, 29.17, 32.03, 33.01, 34.76, 41.78, 42.88, 100.71, 100.97, 106.36, 106.62, 108.05, 108.83, 116.89, 119.03, 119.22, 119.55, 121.11, 134.17, 135.34, 145.67, 147.25, 147.62, 147.81, 206.74 [CO of (**4**)], 208.44 [CO of (**10**)], and 210.44 [CO of (**5a**)].

The ketone (**5b**). To a solution of compound (**4b**) (644 mg, 2.0 mmol) in absolute ethanol (10 ml) was added zinc (powdered; 650 mg, 10 mg-atom) and fused zinc chloride (1.36 g, 10 mmol) and the mixture was heated at reflux for 12 days. Usual work-up followed by p.l.c. [ether–light petroleum (1:1)] gave the *ketone* (**5b**) as an oil (586 mg, 90%) (Found: C, 77.0; H, 7.6. $C_{21}H_{26}O_3$ requires C, 77.3; H, 8.0%); $\nu_{max.}$ 1 700 and 1 610 cm^{-1}; δ_H 1.90 (4 H, q, *J* 7 Hz, 2 × CH_2), 2.46 (8 H, pentet, *J* 7 Hz, 2 × $COCH_2$ and 2 × $ArCH_2$), 3.75 (6 H, s, 2 × OMe), and 6.90 and 7.20 (8 H, q, of AB, *J* 9 Hz, ArH); δ_C 24.37, 33.14, 40.80, 54.12, 112.73, 128.26, 132.61, 156.85, and 209.66.

The ketone (**7**). (Found: C, 72.6; H, 6.2. $C_{24}H_{26}O_5$ requires C, 73.1; H, 6.6%); $\nu_{max.}$ 1 700 cm^{-1}; δ_H 0.75—2.70 (16 H, m), 5.83 (4 H, s, 2 × OCH_2O), and 6.68 (6 H, br s, ArH); δ_C 25.53, 31.25, 33.07, 35.61, 50.16, 100.71, 108.12, 108.83, 121.11, 136.19, 145.54, 147.55, and 213.70.

The ketone (**9**). (Found: C, 77.0; H, 7.0. $C_{20}H_{22}O_3$ requires C, 77.4; H, 7.1%); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 1.51—3.18 (9 H, m), 3.87 and 3.90 (6 H, 2 × s, 2 × OMe), 6.85 (3 H, s, ArH), and 7.11—8.20 (4 H, m, ArH); δ_C 27.48, 28.65, 30.47, 31.71, 45.74, 54.84, 110.33, 110.85, 119.29, 125.53, 126.31, 127.67, 131.51, 132.16, 133.65, 142.88, 146.19, 147.88, and 199.21.

The ketone (**15a**). (Found: C, 70.4; H, 7.1. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%); $\nu_{max.}$ 1 700 cm^{-1}; δ_H 1.02 (3 H, t, *J* 7 Hz, Me),

2.0 (2 H, m, CH_2), 2.45 (6 H, m), 5.95 (2 H, s, OCH_2O), and 6.55—7.15 (3 H, m, ArH).

The ketone (**17**). M.p. 74—75 °C (Found: C, 77.7; H, 7.4. $C_{20}H_{22}O_3$ requires C, 77.4; H, 7.1%); $\nu_{max.}$ 1 695 and 1 600 cm^{-1}; δ_H 0.81—2.90 (13 H, m), 3.80 (3 H, s, OMe), 6.50—7.41 (4 H, m, ArH); δ_C 24.95; 28.07; 31.12, 33.33, 34.11, 43.90, 49.83, 55.16, 111.17, 114.16, 120.85, 129.30, 143.91, 159.71, and 213.12.

General Procedure for Reductive Cleavage of Cyclopropyl Keto Esters (*see also Table* 2).—To a *ca.* 0.5M solution of the cyclopropyl keto ester in the indicated solvent was added the indicated reagent, and the reaction mixture was heated at reflux under nitrogen for the time indicated. The cooled solution was diluted with chloroform, filtered, and the solvent was removed under reduced pressure. The residue was dissolved in chloroform, washed successively with aqueous hydrochloric acid (5%) and brine, and dried (sodium sulphate). Removal of the solvent under reduced pressure followed by p.l.c. [ether–light petroleum (2:3)] gave the pure product. Descriptive and analytical data for products prepared by this procedure are given below.

The keto ester (**22a**). $\nu_{max.}$ 1 720, 1 670, and 1 600 cm^{-1}; δ_H 1.12 (3 H, t, *J* 7.5 Hz, Me), 2.72 (2 H, d, *J* 7.5 Hz, CH_2CO_2), 3.35 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.80 (1 H, m, ArC*H*), 4.0 (2 H, q, *J* 7.5 Hz, CH_2CO_2), and 6.80—8.11 (10 H, m, ArH); the product was identical (i.r., n.m.r., and t.l.c.) with the specimen prepared as follows.

A mixture of chalcone (300 mg, 1.44 mmol), diethyl malonate (23.1 mg, 1.44 mmol), and piperidine (0.2 ml) in absolute ethanol (1 ml) was heated at reflux for 2 days (followed by t.l.c.). To the cooled solution was added aqueous sodium hydroxide (4M; 10 ml) and the reaction mixture was heated at reflux for 6 h. The cooled mixture was acidified with aqueous hydrochloric acid (10%) and extracted with ether. The extracts were washed with brine, dried (magnesium sulphate), and concentrated. Recrystallisation from methanol gave the corresponding *keto acid* (200 mg), m.p. 155—157 °C (Found: C, 75.6; H, 6.0. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%); δ_H ([$^2H_6$]acetone) 2.80 (2 H, d, *J* 7.5 Hz, CH_2CO_2), 3.45 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.80 (1 H, m, ArCH), and 7.11—8.10 (11 H, ArH + CO_2H).

Esterification [absolute ethanol, conc. hydrochloric acid (cat. amount), reflux, 12 h] of the above product gave the keto ester (**22a**), identical (i.r., n.m.r., and t.l.c.) with the above sample.

The keto ester (**22b**). $\nu_{max.}$ 1 720, 1 680, and 1 600 cm^{-1}; δ_H 1.15 (3 H, t, *J* 7.5 Hz, Me), 2.73 (2 H, br d, *J* 7.5 Hz, CH_2CO_2), 3.35 (2 H, d, *J* 7 Hz, $COCH_2$), 3.79 and 3.85 [6 H, 2 × s, 2 × OMe; one proton (ArCH) is beneath the peaks], 4.12 (2 H, q, *J* 7.5 Hz, CO_2CH_2), and 6.81—7.75 (8 H, m, ArH).

Saponification (aq. 5% KOH, MeOH, reflux, 3 h) of this keto ester gave the corresponding *keto acid* as a solid, m.p. 144—145 °C (from MeOH) (Found: C, 69.3; H, 6.1. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.1%); $\nu_{max.}$ 3 100br, 1 690br, and 1 600 cm^{-1}; δ_H 2.75 (2 H, br d, *J* 7 Hz, CH_2CO_2), 3.35 (2 H, d, *J* 7 Hz, $COCH_2$), 3.76 and 3.81 [6 H, 2 × s, 2 × OMe; a proton (ArCH) is beneath the peaks], 6.81—7.75 (8 H, m, ArH), and 8.50 (1 H, br s, OH).

The keto ester (**22c**). (Found: C, 65.9; H, 5.6. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.2%); $\nu_{max.}$ 1 720, 1 675, and 1 600 cm^{-1}; δ_H 1.17 (3 H, t, *J* 7.5 Hz, Me), 2.70 (2 H, br d, *J* 7.5 Hz, CH_2CO_2), 3.25 (2 H, d, *J* 7 Hz, $COCH_2$), 3.81 (1 H, m, ArCH), 4.09 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 5.96 and 6.18 (4 H, 2 × s, 2 × OCH_2O), and 6.70—7.71 (6 H, m, ArH).

Saponification of ester (**22c**) gave the corresponding *keto acid*, m.p. 154—155 °C (Found: 63.7; H, 4.6. $C_{19}H_{16}O_7$ requires C, 64.0; H, 4.5%); $\nu_{max.}$ 3 200br, 1 700, 1 675, and 1 600 cm^{-1}; δ_H ([$^2H_6$]acetone) 2.70 (2 H, dd, CH_2CO_2), 3.35 (2 H, d, *J* 7 Hz, $COCH_2$), 3.75 (1 H, sextet, ArCH), 6.0 (2 H, s, OCH_2O), 6.18 (2 H, s, OCH_2O), and 6.71—7.81 (6 H, m, ArH).

The keto ester (**22d**). $\nu_{max.}$ 1 720, 1 615, and 1 600 cm^{-1}; δ_H 1.15 (3 H, t, *J* 7.5 Hz, Me), 2.75 (2 H, d, *J* 7.5 Hz, CH_2CO_2), 3.30 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.70 (1 H, m, ArCH), 3.82 and 3.90 (6 H, 2 × s, 2 × OMe), 4.11 (2 H, q, *J* 7.5 Hz, CO_2CH_2), and 6.71—7.80 (6 H, m, ArH).

Saponification of ester (**22d**) gave the corresponding *keto acid*, m.p. 151—152 °C (Found: C, 64.6; H, 6.2. $C_{21}H_{24}O_7$ requires C, 64.9; H, 6.2%); $\nu_{max.}$ 3 300br, 1 710, 1 670, and 1 600 cm^{-1}; δ_H 2.65 (2 H, d, *J* 7.5 Hz), 3.20 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.80 and 3.85 [6 H, 2 × s, 2 × OMe; a proton (ArCH) is beneath the peaks], 6.60—7.81 (6 H, m, ArH), and 9.0 (1 H, br s, OH).

The keto ester (**22e**). (Found: C, 63.7; H, 6.0. $C_{23}H_{26}O_8$ requires C, 64.2; H, 6.0%); $\nu_{max.}$ 1 725, 1 670, and 1 600 cm^{-1}; δ_H 1.18 (3 H, t, *J* 7.5 Hz, Me), 2.75 (2 H, d, *J* 7.5 Hz, CH_2CO_2), 3.25 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.75 (1 H, m), 3.86 (9 H, s, 3 × OMe), 4.14 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 6.10 (2 H, s, OCH_2O), 6.55 (2 H, s, ArH), and 6.71—7.80 (3 H, m, ArH).

The Dimeric Ketone (**33**). To a solution of the chalcone (**31**)[18] (400 mg, 1.59 mmol) in a mixture of methanol (20 ml) and ether (4 ml) were added zinc (powdered; 310 mg, 4.8 mg-atom) and fused zinc chloride (648 mg, 4.8 mmol) and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with chloroform, filtered, and the solvent was removed under reduced pressure. The residue was dissolved in chloroform, washed successively with aqueous hydrochloric acid (5%) and water, dried (sodium sulphate), and evaporated. Recrystallisation of the crude product from ether gave the *dimer* (**33**) (210 mg, 50%), m.p. 214—215 °C (Found: C, 80.8; H, 6.8%; M^+, 500. $C_{34}H_{34}O_4$ requires C, 80.6; H, 6.7%; *M*, 506); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 2.35 (6 H, s, 2 × Ar*Me*), 3.07 (4 H, br d, 2 × $COCH_2$), and 3.49 (2 H, br d, 2 × ArCH).

P.l.c. [ether–light petroleum (2:3)] of the mother-liquor gave the ketone (**32**) (32 mg, 8%); $\nu_{max.}$ 1 670 and 1 600 cm^{-1}; δ_H 2.42 (3 H, s, Ar*Me*), 3.20 (4 H, symmetrical m, 2 × CH_2), 3.82 (3 H, s, OMe), 6.98 and 8.00 (4 H, q of AB, *J* 10 Hz, ArH), and 7.40 (4 H, m, ArH); the compound was identical (i.r., n.m.r., and t.l.c.) with a known specimen[23] prepared by catalytic hydrogenation (Adams catalyst) of the chalcone (**31**).

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