Lewis Acid-catalysed Reactions of Aryl Cyclopropyl Ketones. Scope and Mechanism

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The effects of aryl substituents on the stannic chloride-catalysed cyclisation of aryl cyclopropyl ketones (1) to aryl tetralones (2) are consistent with the formation of a benzyl carbocation intermediate (8) or a cyclic oxonium ion intermediate (12). The secondary alcohols (3), occasionally formed as side-products, are derived from this intermediate. Tetralone formation by a concerted pathway is disproved.

THE acid-catalysed nucleophilic ring opening of cyclopropyl ketones has long been of synthetic interest [1-5] and mechanistic importance.[1,6-9] In general it has been found that ring-opening in a cyclopropyl carbocation occurs towards that carbon atom which bears those substituents best able to stabilise a positive charge.[7,10] In conformationally rigid cyclopropyl ketones, geometrical arrangements also play an important role in controlling the preferred mode of cleavage,[7,8,11,12] as do the acid strength, the nucleophilic reactivity, and the reaction medium in deciding the course of the reaction.[8,9,12,13]

Only a few examples of intramolecular cyclisation of aryl cyclopropyl ketones are known [14-17] and these are mechanistically 'confusing'.[18]

We have shown that Lewis acids catalyse the cyclisation of aryl cyclopropyl ketones (1) to aryltetralones (2) and have applied this reaction successfully to the synthesis of picropodophyllone.[19] However, the 4-hydroxyketone (3) was occasionally formed as the main side-product. In addition, arylnaphthalenes (4; R^3 = CO_2Et) were also observed in some instances. These results not only seriously limit the synthetic value of the cyclisation to aryltetralones (2) but also, in the light of previous studies,[9,14-17] make the mechanism unclear.

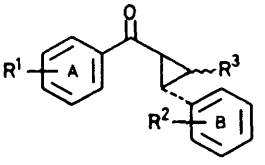
In an effort to learn more about this reaction, the Lewis acid-catalysed reactions of a variety of the cyclopropyl ketones (1) and related compounds have been examined.

Synthesis of Starting Cyclopropyl Ketones.—Compounds (1a—e) were prepared in high yield from the corresponding chalcones using dimethyloxosulphonium methylide in dimethyl sulphoxide at room temperature as previously described.[11]

Using the modified method [19,20] the compounds (1f—k) were prepared in high yield from the corresponding chalcones and ethoxycarbonyldimethylsulphonium methylide as a *ca.* 1 : 1 mixture of (1; R^3 = β-CO_2Et) and (1; R^3 = α-CO_2Et) which was separable by preparative t.l.c.

As previously noted,[19] the stereochemistry of these epimers was unambiguously assigned on the basis of n.m.r. coupling constants and by comparison with known, closely related compounds.[21] A simple means of determining the isomeric ratios in the crude product was therefore at hand. Unexpectedly the R_F value of (1; R^3 = β-CO_2Et) is higher [21] than that of (1; R^3 = α-CO_2Et).

Attempts to prepare the cyclopropyl ketone (7) from



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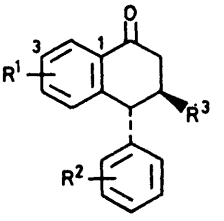

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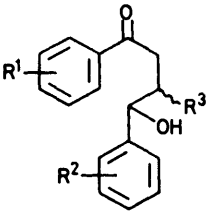

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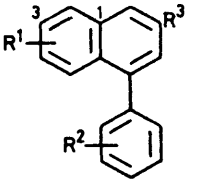

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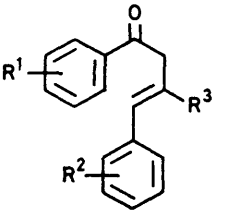
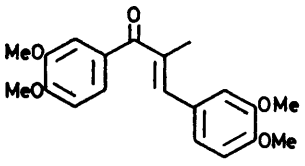


(5)

	R^1	R^2	R^3
(a)	H	H	H
(b)	3-OMe	4-OMe	H
(c)	4-OMe	3,4-$(OMe)_2$	H
(d)	3,4-$(OMe)_2$	3,4-$(OMe)_2$	H
(e)	3,4-$(OMe)_2$	3,4-OCH_2O	H
(f)	3-OMe	4-OMe	CO_2Et
(g)	3,4-$(OMe)_2$	3,4-$(OMe)_2$	CO_2Et
(h)	3,4-$(OMe)_2$	3,4-OCH_2O	CO_2Et
(i)	3,4-OCH_2O	3,4-$(OMe)_2$	CO_2Et
(j)	3,4-OCH_2O	3,4-OCH_2O	CO_2Et
(k)	3,4-OCH_2O	3,4,5-$(OMe)_3$	CO_2Et

the methylchalcone (6) as a route to galbulin,[22] under the usual conditions and prolonged reaction times, failed. Only trace quantities of compound (7) were observed and the chalcone (6) was recovered. This result is probably due to steric effects caused by the presence of the methyl group in the ketone (7).[23]



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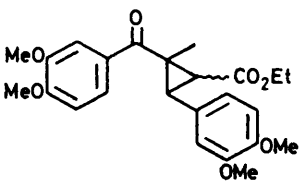


(7)

Lewis Acid-catalysed Reactions.—(*a*) *Scope.* Preliminary results on the cyclisation of cyclopropyl ketones indicated that stannic chloride in methylene chloride, benzene, and nitromethane at room temperature was an effective reagent. Results, however, seemed to depend on the structure and substituents of the cyclopropyl ketone used. Therefore, a large number of aryl cyclopropyl ketones, with a variety of substituents in the aromatic and cyclopropyl rings, were examined. The results are summarised in Table 1.

TABLE 1

Reaction of aryl cyclopropyl ketones with stannic chloride at room temperature

Entry	Reactant	Conditions [a] Solvent, time (h)	Product yield (%) [b] (2)	(3)	(4)	(5)
1	(1a)	CH_2Cl_2, 5		85		
2		$MeNO_2$, 1		90		
2a		$MeNO_2$, 72		90		
3	(1b)	CH_2Cl_2, 8	80			
4		PhH, 8	70			
5		$MeNO_2$, 1	90			
6	(1c)	PhH, 10		70		
7	(1d)	PhH, 10	15	60		
8		$MeNO_2$, 10	80			
9	(1e)	PhH, 47	35	36		
10	(1f)	CH_2Cl_2, 8	80			
11		PhH, 8	80			
12		$MeNO_2$, 1	90			
13	(1g)	CH_2Cl_2, 50	40	16		
14		$MeNO_2$, 45	90			
15	(1h)	CH_2Cl_2, 60	48	39	5	
16		$MeNO_2$, 70	80		trace	
17	(1i)	$MeNO_2$, 70	62		29	
18	(1j)	CH_2Cl_2, 55	trace	26	trace	37
19		$MeNO_2$, 120	70		6	
20	(1k)	CH_2Cl_2, 72		89	trace	
21		$MeNO_2$, 96	53	39	trace	
22 [c]		$MeNO_2$, 360	57	10	9	
23 [c]		$EtNO_2$, 360	57		30	

[a] A 50—100 mM-solution of reactant in the indicated solvent was treated with 1.5 mol equiv. of $SnCl_4$ under nitrogen. [b] Isolated pure yields. [c] $BF_3{\cdot}Et_2O$ (1.5 mol equiv.) was used in place of $SnCl_4$.

From the synthetic viewpoint the cyclisation is general, being compatible with a wide range of substituents and functional groups, notably the ethoxycarbonyl group. The isolated yields are generally high. This reaction therefore provides a short and practical route to aryltetralones which, until now, have been difficult to obtain although they are established key intermediates in the synthesis of aryl lignan lactones.[22,24]

Another feature of the cyclisation giving aryltetralones is its regiospecificity. The high yield of compound (2i), a key intermediate in the synthesis of di-isophyllin,[25,26] from the ketone (1i), in which ring B is more reactive [27] than ring A, highlights this characteristic. Classical cyclisation methods [25,28] lead to the tetralone (2h), rather than to its isomer (2i) unless a deactivating and blocking bromine atom is first introduced into the more reactive ring B.

Conversion of compounds (2g), (2h), and (2j) into retrodendrin dimethyl ether,[29] diphyllin [30] and justicidine-A,[30] and taiwanin-E,[25] respectively, take precedence.

For synthetic purposes we found it unnecessary to purify the cyclopropyl ketones prior to acid-catalysed cyclisation. The use of either one or a mixture of cyclopropyl ketoester epimers as the starting material had no effect on the cyclisation. Accordingly, a mixture of epimers was normally used in the cyclisation step.

Efforts to carry out cyclisation on cyclopropyl ketones without a methoxy-group to activate the aromatic ring (ring A) at the point of tetralone ring closure, *e.g.* the ketones (1a) and (1c), failed. The products from these reactions were the alcohols (3).

It was observed that the choice of solvent in certain cases was critical to the success of the cyclisation process [compare entries 7 with 8, 13 with 14, 15 with 16, and 18 with 19, in addition to the case of (1k) which was noted previously,[19] Table 1]. Nitromethane was a significantly better solvent for the cyclisation than any of the others tested. Although previous studies [14,15,31] showed that benzene is the best solvent as far as yield and *o*/*p* regiocontrol are concerned, it dissolves the highly substituted cyclopropyl ketones, *e.g.* (1g—k), with difficulty. This made it undesirable in the present study. The dependence of the course of the reaction on the nature of the solvent is most strikingly shown by a comparison of entries 18 and 19 (Table 1). Both epimers of the ketone (1j) separately gave the same results. The obvious rationalisation of these results is that solvent polarity facilitates the formation of a discrete carbocation intermediate.

(*b*) *Mechanism.* Details of the mechanism were obtained by varying the substituents in the aromatic rings of the substrates and comparing relative rates of reaction (Table 2). Various pairwise comparisons reveal the effect of both R^1 and R^2 on the rate of cyclisation. The relative rates increase with increasing nucleophilicity of the aromatic rings. This effect is generally consistent with the formation of benzyl carbocations (8) and reflects * the ability of the substituents R^2 to stabilise carbocations [compare (1g) with (1h), (1i) with (1j), and (1j) with (1k), Table 2].

In addition, the relative rates of tetralone formation

* Comparison of other results [28] indicate the following relative abilities to stabilise a carbocation and relative rates of electrophilic aromatic substitution: anisole [27] > veratrole > methylenedioxybenzene [27] > benzene.[32,33]

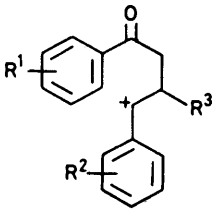
TABLE 2

Effect of substituents on the cyclisation of cyclopropyl ketones (1) with stannic chloride in nitromethane at room tempeature [a]

Reactant	Optimum time [b] (h)	Tetralone (2) yield (%) [c]
(1b)	*ca.* 10 min	90
(1d)	1	80
(1f)	*ca.* 10 min	90
(1g)	45	90
(1h)	70	80
(1i)	70	62
(1j)	120	70
(1k)	15 d	55

[a] All reactions were carried out under nitrogen. A 50—100 mM-solution of the reactant in nitromethane was treated with $SnCl_4$ (1.5 mol equiv.). [b] Followed by t.l.c. [c] Isolated pure yields.

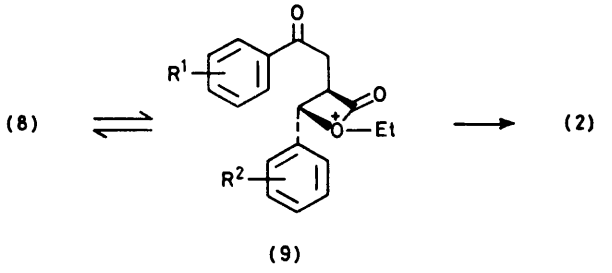
[compare (1b) with (1d), (1f) with (1g), (1g) with (1i), and (1h) with (1j), Table 2] are consistent with the effect of the substituents R^1 on the rate of electrophilic aromatic substitution * and hence with a cationic intermediate such as (8). The occasionally formed side-products (3),



(8)

(4) and (5) (Table 1) also point to the intermediacy of compound (8).

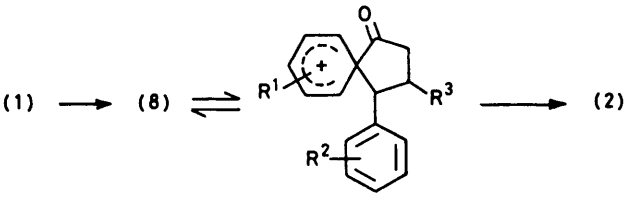
The effect of R^3 (H and CO_2Et) was not detectable by comparing the very reactive ketone (1b) with compound (1f) (Table 2). However, the effect is clearly seen by comparing the compounds (1d) and (1g) (Table 2). The presence of the CO_2Et group reduces the overall rate of cyclisation and probably does so by the inhibition of carbocation (8) formation by its inductive effect.



(9)

SCHEME 1

We have already noted [19] that the tetralones (2; $R^3 = CO_2Et$) are always exclusively *trans*. Although an intermediate such as the ketone (9) can be invoked to explain this, the relative rates of reaction (Table 2) are not consistent with those expected if neighbouring-group participation occurs in the cleavage of the cyclopropane ring by the ethoxycarbonyl group. Therefore direct formation of compound (9) from the ketone (1; $R^3 = CO_2Et$) can be excluded. However, an equilibration between the ketones (8) and (9) (Scheme 1) is reasonable, though not mandatory, for the following reason. We have noted previously [19] that the ketone (1k; $R^3 = \beta$-CO_2Et) rapidly epimerises in nitromethane in the presence of stannic chloride, and it therefore seems probable that, even if some of the *cis*-isomer of compound (2; $R^3 = CO_2Et$) had been formed initially, it would isomerise readily to the more stable *trans*-form and would not be detected.



SCHEME 2

If spiro-intermediates (Scheme 2) were involved in the course of tetralone formation, the ketone (1c) and related compounds [11] would be expected to undergo reaction leading readily to the tetralone (2c). This does not occur, the alcohol (3c) being formed exclusively. This mechanism (Scheme 2) is thereby discounted.

Although superficially straightforward, close examination of this cyclisation revealed that a series of incidents intervened during the conversion of the ketone (1) into the tetralone (2). The effect of time on the reactions of a number of cyclopropyl ketones is shown in Table 3.

TABLE 3

Effect of the reaction time on the reaction of cyclopropyl ketones (1) with stannic chloride at room temperature [a]

Entry	Reactant	Solvent	Time (h)	Product yield (%) (2) : (3) : (4) : (5)
1	(1j)	$MeNO_2$	0.3	Trace : Main : 0 : 0 [b]
2		$MeNO_2$	0.5	Trace : Main : 0 : 0 [b]
3		$MeNO_2$	3	Minor : Main : Trace : Trace [b]
4		$MeNO_2$	12	25 : 61 : 5 : 0 [c]
5		$MeNO_2$	45	30 : 50 : 6 : 0 [c]
6		$MeNO_2$	72	Main : Minor : Trace : 0 [b]
7		$MeNO_2$	120	70 : 0 : 7 : 0 [c]
8	(1g)	$MeNO_2$	1	Trace : Main : 0 : 0 [b]
9		$MeNO_2$	40	Main : Trace : 0 : 0 [b]
10		$MeNO_2$	45	90 : 0 : 0 : 0 [c]
11	(1h)	CH_2Cl_2	40	32 : 40 : Trace : 0 [c]
12		CH_2Cl_2	67	46 : 30 : 5 : 0 [c]
13		$MeNO_2$	7	Minor : Main : Trace : 0 [b]
14		$MeNO_2$	30	1 : 1 : Trace : 0 [b]
15		$MeNO_2$	68	80 : 0 : Trace : 0 [c]
16	(1k)	$MeNO_2$	19	Minor : Main : Trace : 0 [b]
17		$MeNO_2$	96	53 : 39 : Trace : 0 [c]
18		$MeNO_2$	360	50 : 30 : Trace : 0 [c]

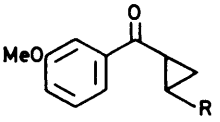
[a] All reactions were performed under nitrogen. A 50 mM-solution of reactant in nitromethane was treated with $SnCl_4$ (1.5 mol equiv.). [b] H.p.t.l.c. determinations compared with authentic samples. [c] Isolated pure products.

Although the alcohols (3) have not been isolated exclusively under these conditions, it is evident from the results in Table 3 that the main products (2) and (3) almost certainly arise from the same intermediate.[34] It

* See footnote on preceding page.

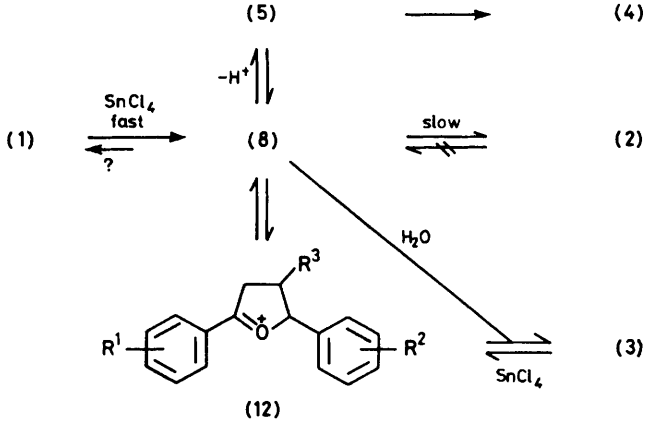
is also apparent that the ketone (1j) rapidly produces an intermediate which gives the alcohol (3j) when trapped[9,35] by water during work-up. This intermediate slowly cyclises to the tetralone (2) upon extended treatment with stannic chloride and longer reaction time (entries 1—7, Table 3).

The most reasonable mechanistic pathways to account for the above results are outlined in Scheme 3.



(10); R = Bu^t
(11); R = H

An intermediate such as the carbocation (8) also accounts for the formation of compounds (2) and (3) and for the reactivities of the ketones (1a)—(1k) relative to the ketones (10) and (11) which do not react.[11] In addition, the intermediate (12) is suggested. Such intermediate ions are well established,[9,35-37] when hydrolysed yield 4-hydroxyketones, and are readily formed by acid treatment of 4-hydroxyketones.[9,35] This theory is supported by the fact that when the alcohol (3j) was

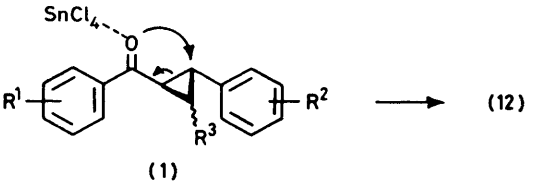


SCHEME 3

treated with stannic chloride under standard conditions, as would be expected with the proposed involvement of the intermediate (12), the tetralone (2j) was formed. Since direct formation of the tetralone (2) from the cyclic oxonium ion (12) is sterically improbable the equilibrium (8) ⇌ (12) is considered. The anomalously long life of a number of the intermediate carbocations (see Table 3) can be readily explained by this equilibrium as can the effect of solvent and of aryl substituents.

The rate of tetralone (2) formation is increased in more polar solvents and with increasing nucleophilicity of the aromatic nucleus, as previously noted. These effects are consistent with a shift in the equilibrium between intermediates (8) and (12) leading to an increased concentration of the benzyl carbocation (8) with a consequent increase in the rate of formation of the tetralone (2).

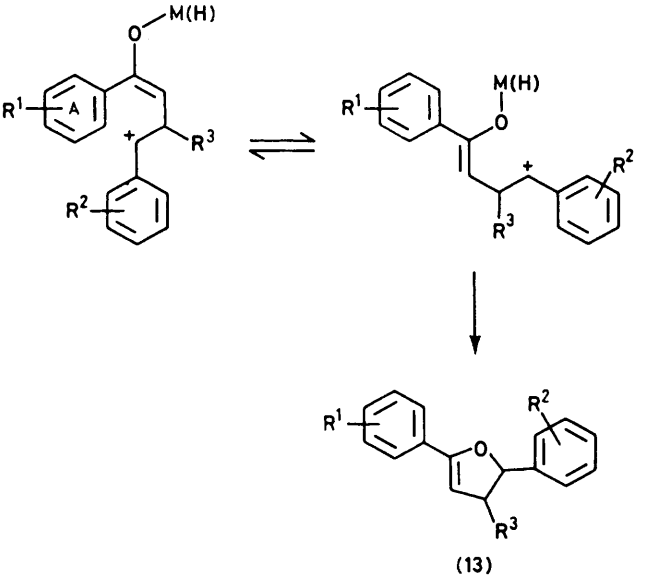
It remains to be shown which of the intermediates (8) and (12) is initially formed. Although it is not readily apparent from the above results, an inspection of models indicates that the direct formation of the oxonium ion (12) from the ketone (1) by concerted neighbouring



(1)

ketone group participation is sterically unlikely. Accordingly, a mechanism in which the intermediate (8) is formed first [from the ketone (1)] is preferred.*

A further point remains to be clarified. Ring A in compound (1) and in subsequent products is deactivated by the α-carbonyl group. If cyclisation involved the enol or enolate of the carbocation (8) this would facilitate tetralone formation. However, *E*/*Z* isomerisation might be expected (Scheme 4) as might the collapse of the *Z*-enol



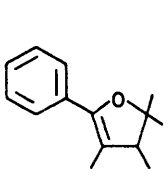
SCHEME 4

or -enolate to the corresponding dihydrofuran derivative (13). No such intermediate has been detected by the present work. In addition, the fact that the related dihydrofuran (14) is stable towards aluminium chloride[36] seems to preclude the pathways indicated in Scheme 4. On the other hand, the dihydrofuran (13) could not be expected if the *E*-enol or -enolate were formed exclusively and its isomerisation inhibited by Sn^{IV} chelation as in compound (15).

In conclusion, the evidence obtained to show that the Lewis acid-promoted cyclisation of cyclopropyl ketones

* We consider that the intermediate (8) arises through protonation by nitromethane [$MeNO_2$: pK_a; intermediate (8) : pK_a *ca.* 20, calculated by comparison with acetophenone[38]].

proceeds by way of a stepwise cationic reaction. While the evidence is not entirely conclusive, all the side-reactions discussed here, as well as the effects of solvent and substituents, may be explained by this mechanism. However, none of the data available preclude the direct participation of an aryl ring *via* a concerted cyclisation of



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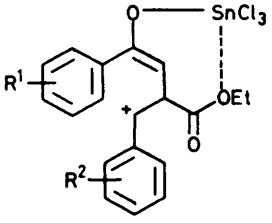
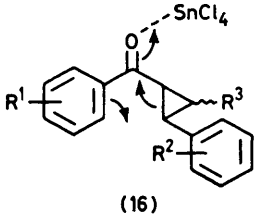


(15)

the ketone (16) as the major route in the case of the highly reactive cyclopropyl ketones such as (1b) and (1f) (see Table 2). In addition, this concerted mechanism might also be the minor route in the case of the less reactive cyclopropyl ketones.

Compounds (2; $R^3 = CO_2Et$) are well established synthetic precusors of aryl lignan lactones [29,39] and arylnaphthalene lignans.[30] The naphthalenes (4) are potential precursors of arylnaphthalene lignans,[22,39a] while the suitably substituted products (3) and (6) are potential precursors of 1,4-diarylbutane lignans.[22,39a]



(16)

EXPERIMENTAL

General procedures, unless otherwise stated, were as detailed previously.[11,19] ^{13}C N.m.r. spectra were recorded in $CDCl_3$ on a JEOL FX60 instrument. Compounds (1a)—(1f) and (1k) were synthesised from the corresponding chalcones as previously described.[11,19,40] The products (2b), (3c), (2d), (3d), (2e), (2f), (2k), (3k), and (4k) have been characterised previously.[11,19]

The Cyclopropyl Ketoesters (1g)—(1i).—These were prepared according to the general procedure previously detailed.[19] Their yields, analytical results, and physical properties are given below.

Ethyl 2-(3,4-*Dimethoxybenzoyl*)-3-(3,4-*dimethoxyphenyl*)-*cyclopropane*-1-*carboxylate* (1g).—The *ester* was prepared in 87% yield as an approximately 1 : 1 mixture of isomers (n.m.r.) [preparative layer chromatography (p.l.c.), diethyl ether–light petroleum 1 : 1] (Found: C, 66.5; H, 6.0. $C_{23}H_{26}O_7$ requires C, 66.7; H, 6.3%); $\nu_{max.}$ 1 725, 1 660, and 1 600 cm^{-1}; δ 1.11 and 1.31 (3 H, 2 × t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.50—3.61 (3 H, m, cyclopropyl H), 3.90 (6 H, s, 2 × OMe), 3.99 (6 H, s, 2 × OMe), 4.15 (2 H, m, CO_2CH_2), and 6.7—8.0 (6 H, m, ArH).

Ethyl 2-(3,4-*Dimethoxybenzoyl*)-3-(3,4-*methylenedioxyphenyl*)*cyclopropane*-1-*carboxylate* (1h).—P.l.c. (diethyl ether–light petroleum 3 : 2) gave two bands. The first band (higher R_F) gave the *isomer* (R = β-CO_2Et) of (1h) as an oil (52%) (Found: C, 65.7; H, 5.5. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.6%); $\nu_{max.}$ 1 725, 1 665, and 1 600 cm^{-1}; δ 1.12 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.75 (1 H, dd, *J* 5 and 11 Hz), 3.15 (1 H, dd, *J* 5 and 6 Hz), 3.3 (1 H, dd, *J* 4.5 and 6 Hz), 3.98 (6 H, s, 2 × OMe), 4.05 (2 H, CO_2CH_2), 5.98 (2 H, s, OCH_2O), and 6.71—7.91 (6 H, m, ArH). The band of lower R_F gave the *epimer* of (2h) (40%) as an oil; $\nu_{max.}$ 1 725, 1 670, and 1 600 cm^{-1}; δ 1.15 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.51 (1 H, dd, *J* 6 and 10 Hz), 3.02 (1 H, dd, *J* 7 and 10 Hz), 3.30 (1 H, dd, *J* 5 and 7 Hz), 3.94 (6 H, s, 2 × OMe), 4.12 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 5.98 (2 H, s, OCH_2O), and 6.8—7.81 (6 H, m, ArH).

Ethyl 3-(3,4-*Dimethoxyphenyl*-2-(3,4-*methylenedioxybenzoyl*)*cyclopropane*-1-*carboxylate* (1i).—The ketoester (1i) was isolated as an approximately 1 : 1 isomeric mixture in 90% yield (p.l.c., diethyl ether–light petroleum 3 : 2) as an oil (Found: C, 66.0; H, 5.3. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.6%); $\nu_{max.}$ 1 720, 1 660, and 1 600 cm^{-1}; δ 1.21 (3 H, $CO_2CH_2CH_3$), 2.51—3.60 (3 H, m), 3.79 and 3.88 (6 H, 2 × s, 2 × OMe), 4.20 (2 H, CO_2CH_2), 6.08 and 6.10 (2 H, 2 × s, OCH_2O), and 6.71—7.81 (6 H, m, ArH).

Ethyl 2-(3,4-*Methylenedioxybenzoyl*)-3-(3,4-*methylenedioxyphenyl*)*cyclopropane*-1-*carboxylate* (1j).—P.l.c. (diethyl ether–light petroleum 3 : 2) of the crude oily product gave two bands. The band of higher R_F afforded the ketoester *isomer* (R = β-CO_2Et) (42%) (1j) as an oil; $\nu_{max.}$ 1 720, 1 665, and 1 600 cm^{-1}; δ 1.10 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.24 (1 H, dd, *J* 5 and 10 Hz), 3.2 (1 H, dd, *J* 5 and 6 Hz), 3.38 (1 H, dd, *J* 4.5 and 6 Hz), 4.05 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 6.01 (2 H, s, OCH_2O), 6.81—7.90 (6 H, m, ArH). The band of lower R_F gave the *epimer* of the ketoester (1j) (48%) (Found: C, 65.5; H, 4.2. $C_{21}H_{18}O_7$ requires C, 66.0; H, 4.7%); $\nu_{max.}$ 1 720, 1 665, and 1 600 cm^{-1}; δ 1.15 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.50 (1 H, dd, *J* 6 and 10 Hz), 2.95 (1 H, dd, *J* 7 and 10 Hz), 3.28 (1 H, dd, *J* 6 and 7 Hz), 4.12 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 5.99 (2 H, s, OCH_2O), 6.08 (2 H, s, OCH_2O), and 6.71—7.80 (6 H, m, ArH).

Lewis Acid-catalysed Reactions of Cyclopropyl Ketones and Cyclopropyl Ketoesters.—These were performed according to the general procedure previously described.[11,19] Products were separated by p.l.c. (diethyl ether–light petroleum). The physical and chemical properties and analytical data of the products obtained are described below.

6,7-*Dimethoxy*-4-(3,4-*dimethoxyphenyl*)-3-*ethoxycarbonyl*-3,4-*dihydronaphthalene*-1(2H)-*one* (2g), m.p. 130—131 °C (MeOH) (lit.,[38a,41] m.p. 130—131 °C, 132—134 °C); $\nu_{max.}$ 1 720 and 1 670 cm^{-1}; δ (CCl_4) 1.03 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.70 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.21 (m, 1 H, $CHCO_2$), 3.71, 3.78, 3.82, and 3.90 (2 H, 4 × s, 4 × OMe), 4.0 (part of q, *J* 7.5 Hz, CO_2CH_2), 4.42 (1 H, d, *J* 7.5 Hz, ArCH), 6.47 (1 H, s, ArH), 6.75 (3 H, m, ArH), and 7.50 (1 H, s, ArH).

6,7-*Dimethoxy*-3-*ethoxycarbonyl*-4-(3,4-*methylenedioxyphenyl*)-3,4-*dihydronaphthalene*-1(2H)-*one* (2h),[30] m.p. 137—138 °C (MeOH) (Found: C, 65.3; H, 5.8. Calc. for $C_{22}H_{22}O_7$: C, 66.3; H, 5.6%); $\nu_{max.}$ 1 720 and 1 670 cm^{-1}; δ 1.10 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.35 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.30 (1 H, m, $CHCO_2$), 3.81 and 3.98 (6 H, 2 × s, 2 × OMe), 4.11 (2 H, q, partly overlapped with OMe group, *J* 7.5 Hz, CO_2CH_2), 4.62 (1 H, d, *J* 7.5 Hz, ArCH), 6.0 (2 H, s, OCH_2O), 6.50—7.01 (4 H, m, ArH), and 7.65 (1 H, s, ArH).

4-(3,4-*Dimethoxyphenyl*)-3-*ethoxycarbonyl*-6,7-*methylenedioxy*-3,4-*dihydronaphthalene*-1(2H)-*one* (2i), m.p. 129—131 °C (CH_2Cl_2–hexane) (Found: C, 65.9; H, 5.5. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.6%); $\nu_{max.}$ 1 720 and 1 670 cm^{-1}; δ 1.06 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.85 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.35 (1 H, m, $CHCO_2$), 3.87 and 3.89 (6 H, 2 × s, 2 × OMe), 4.06 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 4.55 (1 H, d, *J* 7.5 Hz, ArCH), 6.02 (2 H, s, OCH_2O), 6.45 (1 H, s, ArH), 6.75—7.45 (3 H, m, ArH), and 7.58 (1 H, s, ArH).

3-*Ethoxycarbonyl*-6,7-*methylenedioxy*-4-(3,4-*methylenedioxyphenyl*)-3,4-*dihydronaphthalene*-1(2H)-*one* (2j), m.p. 125—127 °C (MeOH) (lit.,[25] m.p. 122—124 °C); $\nu_{max.}$ 1 720 and 1 670 cm^{-1}; δ 1.08 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 2.71 (2 H, d, *J* 7.5 Hz, $COCH_2$), 3.15 (1 H, m, $CHCO_2$), 4.0 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 4.42 (1 H, d, *J* 7.5 Hz, ArCH), 6.0 and 6.06 (4 H, 2 × s, 2 × OCH_2O), 6.29 (1 H, s, ArH), 6.65 (3 H, m, ArH), and 7.49 (1 H, s, ArH).

3-*Hydroxy*-3-*phenylpropyl phenyl ketone* (3a),[9] was obtained as an oil; $\nu_{max.}$ 3 400 and 1 660 cm^{-1}; δ 2.25 (2 H, q, *J* 7 Hz, CH_2), 2.8 (1 H, br s, OH, replacement + D_2O), 3.10 (2 H, t, *J* 7 Hz, $COCH_2$), 4.82 (1 H, t, *J* 7 Hz, CH), and 7.31—8.10 (10 H, m, ArH).

3,4-*Dimethoxyphenyl* 3-*hydroxy*-3-(3,4-*methylenedioxyphenyl*)*propyl ketone* (3e), obtained as an oil (Found: C, 66.5; H, 6.4. $C_{20}H_{24}O_6$ requires C, 66.7; H, 6.7%); $\nu_{max.}$ 3 400, 1 670, and 1 600 cm^{-1}; δ 2.14 (2 H, q, *J* 7 Hz, CH_2), 3.04 (2 H, t, *J* 7 Hz, $COCH_2$), 3.93 (6 H, s, 2 × OMe), 4.77 (1 H, m, CH), 6.01 (2 H, s, OCH_2O), and 6.70—7.81 (6 H, m, ArH).

Ethyl 3-(3,4-*dimethoxybenzoyl*)-1-(3,4-*dimethoxyphenyl*)-1-*hydroxypropane*-2-*carboxylate* (3g), obtained as an oil (Found: C, 63.4; H, 6.1. $C_{23}H_{28}O_8$ requires C, 63.9; H, 6.5%); $\nu_{max.}$ 3 450, 1 720, 1 680, and 1 600 cm^{-1}; δ 1.12, 1.21 (3 H, 2 t, *J* 7 Hz, $CO_2CH_2CH_3$), 3.35 (3 H, m), 3.90, 3.93, 3.96 (12 H, 3 × s, 4 × OMe), 4.19 (2 H, m, CO_2CH_2), 5.05 (d, *J* 7 Hz, *threo*-isomer), 5.22 (d, *J* 3 Hz, *erythro*-isomer), and 6.70—7.81 (6 H, m, ArH).

Ethyl 3-(3,4-*dimethoxybenzoyl*)-1-*hydroxy*-1-(3,4-*methylenedioxyphenyl*)*propane*-2-*carboxylate* (3h), m.p. 93—97 °C (Found: C, 63.1; H, 5.4. $C_{22}H_{24}O_8$ requires C, 63.5; H, 5.8%); $\nu_{max.}$ 3 450, 1 720, and 1 680 cm^{-1}; δ 1.12, 1.20 (3 H, 2 × t, *J* 7 Hz, $CO_2CH_2CH_3$), 3.35 (3 H, m), 3.93, 3.97 (6 H, 2 × s, 2 × OMe), 4.21 (2 H, m, CO_2CH_2), 5.0 (d, *J* 7 Hz, ArCHO of the *threo*-isomer), 5.19 (d, *J* 3 Hz, ArCHO of the *erythro*-isomer), 6.02 (2 H, s, OCH_2O), and 6.72—7.80 (6 H, m, ArH).

Ethyl 1-*hydroxy*-3-(3,4-*methylenedioxybenzoyl*)-1-(3,4-*methylenedioxyphenyl*)*propane*-2-*carboxylate* (3j), obtained as an oil (Found: C, 62.8; H, 5.4. $C_{21}H_{20}O_8$ requires C, 63.0; H, 5.0%); $\nu_{max.}$ 3 450, 1 720, 1 670, and 1 600 cm^{-1}; δ 1.10, 1.16 (3 H, 2 × t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 3.25 (3 H, m), 4.02 and 4.08 (2 H, 2 × q, *J* 7.5 Hz, CO_2CH_2), 4.95 (d, *J* 7 Hz, ArCHO of the *threo*-isomer), 5.15 (d, *J* 3 Hz, ArCHO of the *erythro*-isomer), 5.93 and 6.04 (4 H, 2 × s, 2 × OCH_2O), and 6.60—7.70 (6 H, m, ArH).

6,7-*Dimethoxy*-3-*ethoxycarbonyl*-1-(3,4-*methylenedioxyphenyl*)*naphthalene* (4h), m.p. 171—173 °C (Found: C, 69.1; H, 5.0. $C_{22}H_{20}O_6$ requires C, 69.5; H, 5.3%); $\nu_{max.}$ 1 700 and 1 610 cm^{-1}; δ 1.42 (3 H, t, *J* 7.5 Hz, $CO_2CH_2CH_3$), 3.89 and 4.04 (6 H, 2 × s, 2 × OMe), 4.48 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 6.11 (2 H, s, OCH_2O), 7.07 (3 H, s, ArH), 7.38 (2 H, s, ArH), 7.98 (1 H, d, *J* 2 Hz, ArH), and 8.56 (1 H, d, *J* 2 Hz, ArH); δ_C 14.49, 55.94, 61.01, 101.29, 104.74, 107.86, 108.44, 110.33, 123.25, 125.01, 125.72, 128.65, 129.10, 130.21, 131.42, 138.59, 147.10, 147.81, 149.89, 151.39, and 166.98 p.p.m.

Hydrolysis (5% KOH, methanol, reflux 3 h), of the ester (4h), gave 3-carboxy-6,7-dimethoxy(1-3,4-methylenedioxyphenyl)naphthalene (85%), m.p. 276—278 °C (MeOH) (lit.,[42] m.p. 277—278 °C); $\nu_{max.}$ identical with the known compound.

1-(3,4-*Dimethoxyphenyl*)-3-*ethoxycarbonyl*-6,7-*methylenedioxynaphthalene* (4i), m.p. 177—179 °C (Found: C, 69.0; H, 5.6. $C_{22}H_{20}O_6$ requires C, 69.5; H, 5.3%); $\nu_{max.}$ 1 700 and 1 600 cm^{-1}; δ 1.30 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 3.79, 3.85 (6 H, 2 × s, 2 × OMe), 4.34 (2 H, q, *J* 7 Hz, CO_2CH_2), 6.0 (2 H, s, OCH_2O), 7.0 (3 H, ArH), 7.27 (2 H, d, *J* 1.5 Hz, ArH), 7.89 (1 H, s, ArH), and 8.40 (1 H, s, ArH).

3-*Ethoxycarbonyl*-6,7-*methylenedioxy*-1-(3,4-*methylenedioxyphenyl*)*naphthalene* (4j), obtained as an oil (Found: C, 67.8; H, 4.0. $C_{21}H_{16}O_6$ requires C, 69.2; H, 4.4%); $\nu_{max.}$ 1 710 and 1 600 cm^{-1}; δ 1.20 (3 H, t, *J* 7.5 Hz, Me), 4.08 (2 H, q, *J* 7.5 Hz, CO_2CH_2), 6.02 and 6.10 (4 H, 2 × s, 2 × OCH_2O), and 6.5—7.71 (7 H, ArH).

3-(3,4-*Methylenedioxybenzoyl*)-1-(3,4-*methylenedioxyphenyl*)*prop*-1-*ene*-2-*carboxylate* (5j), obtained as an oil (Found: C, 65.6; H, 4.3. $C_{21}H_{18}O_7$ requires C, 66.0; H, 4.7%); $\nu_{max.}$ 1 710, 1 680, and 1 600 cm^{-1}; δ 1.08, 1.12 (3 H, 2 × t, *J* 7 Hz, Me), 4.17 (2 H, s, $COCH_2$), 4.25 (2 H, q, *J* 7 Hz, CO_2CH_2), 6.01 and 6.11 (4 H, 2 × s, 2 × OCH_2O), and 6.71—8.01 (6 H, m, ArH).

[1/1352 *Received*, 21*st August*, 1981]

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