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NUCLEOPHILIC RING OPENING OF EPOXIDES BY CARBANIONS

NOVEL FORMATION OF CYCLOPROPANE DERIVATIVES IN A NON-POLAR SOLVENT

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Abstract—Nucleophilic ring-opening of epoxides **2(a–d)** with carbanions of different steric requirements under refluxing benzene afforded a single stereoisomer of the cyclopropane derivatives **4**. The same reaction under refluxing ethanol gave the normal products, i.e. the *trans*-lactones **6**. Mechanism and high stereoselectivity observed in the novel cyclopropane formation, and regiospecific cleavage of the cyclopropane carboxylic acids (in **4**) have also been discussed in detail.

In connection with our programme for the synthesis of desmotroposantonins, and related lactones (as **1**), we synthesised[1] two stereoisomers of *cis*-1-desmethyldesmotroposantonin methyl ethers[2] as **1a** and **1b** (with *cis*-fused lactone ring). However the need to find a synthesis for the other two *trans*-isomers **1a** and **1b** remained. *Trans*-ring-opening of the epoxide **2a** appeared attractive and the interaction of **2a** with sodium diethylmalonate afforded[3] a mixture of the *cis*-and the *trans*-lactones as a result of the attack of the carbanion at the benzylic C atom. The formation of the *cis*-lactone as the major product[3] revealed that the pathway is not completely S_N2 in character. Furthermore, similar ring opening of **2a** with a more sterically hindered carbanion derived from diethyl methylmalonate afforded[3] the hydroxy ether **3** as the only isolable product. This clearly indicated that the *peri*-Me group in **2a** hinders the approach of the more nucleophilic carbanion to benzylic C atom of **2a**. Ethanol or ethoxide ion, though a weaker nucleophile than carbanion, completes the ring-opening process to furnish the product **3**.

Consequently, the ring-opening of epoxide **2a** with the anion of diethyl methylmalonate in a highly nonpolar solvent such as benzene was investigated. In the absence of another nucleophile, possibly the carbanion would be forced to attack in some measure the alternative position (nonbenzylic C) of the epoxide **2a** to provide the *trans*-lactones **1a** and **1b**. Though this objective was not realised, we report[4] in detail the novel and highly stereoselective formation of cyclopropane derivatives **4** through ring-opening by heating **2a** and other related epoxides **2(b–e)** in benzene under reflux. This study also includes ring-opening of epoxides **2(d–f)** by heating under reflux the same carbanion in ethanol to show the dramatic influence of solvents on the nature of products formed.

RING-OPENING OF EPOXIDES AND BROMOHYDRINS IN REFLUXING BENZENE

Interaction of the epoxide **2a**[3] with the anion of diethyl methylmalonate heated under reflux (30 hr) in benzene afforded the recovered epoxide **2a**, and an ester, characterised as the cyclopropane compound **4a** in moderate yield,† and this on alkaline hydrolysis furnished the crystalline acid **4b**. Careful work-up of the mixture provided the *trans*-hydroxy-acid **5a**[3] in substantial amount.

Similar condensation of the epoxide **2b**,[3] bearing a bulky Br atom at the *peri*-position, also provided a product which on hydrolysis furnished the crystalline cyclopropane acid **4c**.

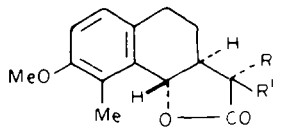
To investigate the generality and stereoselectivity of cyclopropane formation, the studies were extended to other related epoxides such as **2(c–f)**.

The simplest epoxide **2c**[3,5] furnished the desired cyclopropyl derivative **4d** as the major product (47%), and the known[6] *trans*-lactone **6a** as the minor product (7%). This lactone **6a** on alkaline hydrolysis gave the corresponding *trans*-hydroxy-acid **5b** which could be lactonised back to the lactone **6a**. The condensation of the epoxide **2c** with the anion of diethyl methylmalonate in ethanol is known[6] to provide only the lactone **6a**.

3,4-Epoxychroman[7] **2d** similarly afforded in high yield (64%) the cyclopropyl ester **4f**. This ester on hydrolysis provided the crystalline acid **4g**, and this on esterification with diazomethane furnished the crystalline methyl ester **4h**.

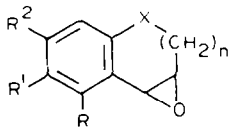
In order to study the effect of the more flexible heterocyclic ring on the course of ring-opening, the epoxide **2e** was prepared from the *trans*-bromohydrin **7c** which was available from the styrene **8a**[8] following the procedure of Dalton *et al.*[9] Interaction of the epoxide **2e** with the anion of diethyl methylmalonate in benzene as before afforded mainly the *trans*-lactone **6b** (63%), and the desired cyclopropyl carboxylic acid **4i**, purified through its methyl ester **4j** but in very low yield (5%). The crystalline acid **4i** was isolated in a better yield (10%) when the above condensation was carried out in presence of some diethyl carbonate.

†This reaction under refluxing dimethoxyethane (DME) afforded in comparable yield the crystalline acid **4b** (see Experimental).



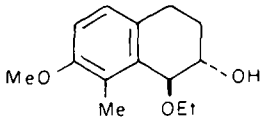
1

a. R = Me, R' = H
b R = H, R' = Me



2

	R	R'	R²	X	n
a	Me	OMe	H	CH_2	1
b	Br	OMe	Me	CH_2	1
c	H	H	H	CH_2	1
d	H	H	H	O	1
e	H	H	H	O	2
f	H	H	H	CH_2	2



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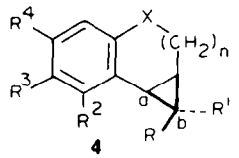


4

	R	R'	R²	R³	R⁴	X	n
a	Me	CO_2Et	Me	OMe	H	CH_2	1
b	Me	CO_2H	Me	OMe	H	CH_2	1
c	Me	CO_2H	Br	OMe	Me	CH_2	1
d	Me	CO_2H	H	H	H	CH_2	1
e	Me	CO_2Me	H	H	H	CH_2	1
f	Me	CO_2Et	H	H	H	O	1
g	Me	CO_2H	H	H	H	O	1
h	Me	CO_2Me	H	H	H	O	1
i	Me	CO_2H	H	H	H	O	2
j	Me	CO_2Me	H	H	H	O	2
k	$CHMe_2$	CO_2Et	H	H	H	CH_2	1
l	$CHMe_2$	CO_2H	H	H	H	CH_2	1
m	$CHMe_2$	CO_2Me	H	H	H	CH_2	1
n	$CHMe_2$	CO_2H	H	H	H	O	1
o	$CHMe_2$	CO_2Me	H	H	H	O	1

Fig. 1.

3,4 - Epoxy - 1,2 - benzocyclohept - 1 - ene **2f** was prepared from the *trans*-bromohydrin **7d**, available from the styrene[10] **8b**. Condensation of **2f** with the carbanion as above furnished only the *trans*-lactone **6c** in excellent yield. This reaction even in the presence of diethyl carbonate failed to give any cyclopropyl derivative.

The 2 - methyl - 3,4 - dihydronaphthalene - 1,2 - oxide **9** was completely recovered unchanged even after heating with the enolate of diethyl methylmalonate in benzene for 25 hr.

Since the *trans*-bromohydrin **7a**,[3] is the precursor of the epoxide **2c**, it was of importance to investigate heating of **7a** with the anion of diethyl methylmalonate in benzene under reflux. This afforded a separable mixture of the lactonic ester **10**, and the *trans*-lactone[6] **6a** in a ratio of *ca.* 1:1. The lactonic ester **10** was shown by ^{1}H-NMR to be a 1;1 mixture of epimers; epimeric at the asymmetric centre carrying the Me and the carbethoxylic groups. No cyclopropyl derivative † could be detected in this reaction.

Similar interaction of the *trans*-bromohydrin **7b**[7] with the carbanion of diethyl methylmalonate resulted in the isolation of the *trans*-lactone **6f** and a diastereomeric mixture of the hydroxy-ester **5d** as the minor and major products, respectively.

The interaction of the more sterically hindered carbanion derived from diethyl isopropylmalonate with 3, 4-dihydronaphthalene - 1,2 - oxide **2c**[3,5] in benzne as above afforded the desired cyclopropane derivative **4k** and the lactone **6d** as the major and minor products. Hydrolysis of the ester **4k** gave the crystalline acid **4l**, and the recovered ester **4k** indicating the hindered nature of the ester function in **4k**. This ester, however, was efficiently hydrolysed by potassium-t-butoxide[11] to furnish a good yield of acid **4l**; and this on esterification with diazomethane provided the crystalline methyl ester **4m**.

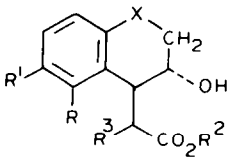
Similar condensation of 3,4-epoxychroman **2d**[7] with the anion of diethyl isopropylmalonate furnished in low yields the cyclopropyl acid **4n**, the *trans*-hydroxy-acid **5e**, and the *trans*-lactone **6e**. This *trans*-lactone **6e** on alkaline hydrolysis afforded the corresponding *trans*-hydroxy-acid **5e** which could be lactonised back to the lactone **6e**.

Attempted condensation of the epoxide **2c** with the more bulkier carbanion from diethyl phenylmalonate in benzene gave mainly the recovered starting materials.

RING-OPENING OF EPOXIDES AND BROMOHYDRIN UNDER REFLUXING ETHANOL

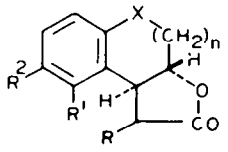
Interaction of 3,4-epoxychroman **2d**[7] with sodium diethyl methylmalonate in ethanol afforded only the hydroxy-ester **5d** as a mixture of diastereomers. Alkaline

†The bromohydrin **7a** in presence of excess carbanion is expected to furnish the epoxide **2c** for further reaction. We fail to understand the reason for the non-formation of cyclopropane compound in this condensation.



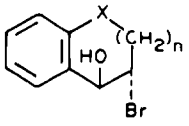
5

	R	R¹	R²	R³	X
a	Me	OMe	H	Me	CH_2
b	H	H	H	Me	CH_2
c	H	H	H	Me	O
d	H	H	Et	Me	O
e	H	H	H	$CH(Me)_2$	O



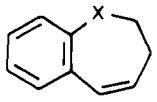
6

	R	R¹	R²	X	n
a	Me	H	H	CH_2	1
b	Me	H	H	O	2
c	Me	H	H	CH_2	2
d	$CHMe_2$	H	H	CH_2	1
e	$CHMe_2$	H	H	O	1
f	α-Me	H	H	O	1
g	β-Me	H	H	O	1



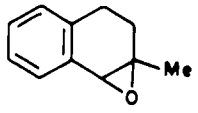
7

a: X = CH_2, n = 1
b: X = O, n = 1
c: X = O, n = 2
d: X = CH_2, n = 2



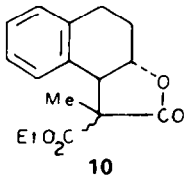
8

a: X = O
b: X = CH_2



9

Fig. 2.



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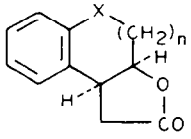
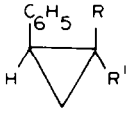


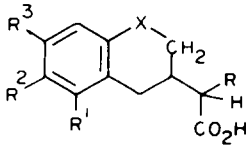
11

	X	n
a	O	2
b	O	1
c	CH_2	2



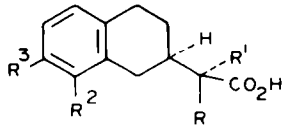
12

a. R = Me, R¹ = CO_2H
b R = CO_2H, R¹ = Me
c R = CO_2H, R¹ = H
d R = H, R¹ = CO_2H



13

	R	R¹	R²	R³	X
a	Me	Me	OMe	H	CH_2
b	Me	H	OMe	Me	CH_2
c	Me	H	H	H	CH_2
d	Me	H	H	H	O
e	$CHMe_2$	H	H	H	CH_2
f	$CHMe_2$	H	H	H	O



14

	R	R¹	R²	R³
a	Me	H	Me	OMe
b	H	Me	H	H

Fig. 3.

hydrolysis of this mixture gave an oily acid which was heated at 160° to provide neutral and acidic products. The former was characterised as the *trans*-lactone **6f**, m.p. 118–119° and the acid part on keeping partially solidified to furnish a pure isomer of the *trans*-hydroxy-acid **5c**. This pure acid on heating at 160° partially lactonised to provide an isomeric *trans*-lactone **6g**, m.p. 116–117° and the recovered crystalline acid **5c**. Alkaline hydrolysis of the lactone **6f** furnished an isomeric mixture of the *trans*-hydroxy-acid **5c** from which a pure isomer was isolated. Similar hydrolysis of the isomeric lactone **6g** provided the same pure isomer of **5c** in good yield. The two lactones **6f** and **6g** differ only in the stereochemistry at the C carrying the Me group. This was proved by heating **6f** with anhydrous potassium carbonate[2,12] in xylene when it was recovered unchanged whereas the isomeric lactone **6g** on similar treatment gave a mixture (from ^{1}H-NMR) of the isomeric lactones **6f** and **6g**. This mixture on fractional crystallisation finally afforded a pure sample of the thermodynamically more stable lactone **6f**. Inspection of the Dreiding molecular model of these lactones **6(f–g)** reveals that the Me group in **6g** is relatively more shielded by the phenyl ring than the corresponding Me group in **6f**, and as a consequence, the Me group in **6g** showed a doublet at higher field (τ 8.73) than the Me group (τ 8.42) in **6f**.

trans-Bromohydrin **7c**, the precursor of the epoxide **2e** on heating with excess sodium diethyl methylmalonate in ethanol provided a neutral product which on alkaline hydrolysis and subsequent lactonisation afforded in excellent yield the *trans*-lactone **6b**.

Similar condensation of the bromohydrin **7d** furnished the *trans*-lactone **6c** in high yield.

The alkaline hydrolysis of the lactones **6b** and **6c**, and careful acidification resulted only in the recovery of the starting lactones.

Stereochemistry of the lactones

The *trans*-ring-fusion of the lactones **6(a–g)** follows from the fact that epoxide ring-opening by malonate anions proceeds[6] in a *trans-diaxial* fashion. The Me group α to the lactone C=O is generally assumed to have the most stable configuration, i.e. *quasi-equatorial*. Further support for the *trans*-stereochemistry of the lactones is available from the chemical shift of the H attached to the alkoxy-C of the lactone. This hydrogen in the *trans*-isomer is relatively more shielded by the ring current of the benzene ring than that in the *cis*-isomer. Chemical shifts for these hydrogens of some of the *trans*-lactones, and the related *cis*-lactones[13] **11** are summarised in Table 1.

MECHANISM AND STEREOSELECTIVITY OF NOVEL CYCLOPROPANE FORMATION

In all cases of epoxide ring-opening with carbanions by heating in benzene, only a single stereoisomer of cyclopropyl derivative with the carboxylic function *trans* to the phenyl ring was formed. The assignments of the stereochemistry mainly follow from their ^{1}H-NMR spectra. The signals for the Me groups attached to the cyclopropane ring C are presented in Table 2. Comparing the Me signals with those of the known[14] related cyclopropyl compounds **12a** and **12b**, it is quite reasonable to predict that the Me group in each case is shielded by the ring current of the phenyl ring.

The UV spectrum[15] of the *trans*-compound **12d** has a maximum at slightly higher wavelength than the *cis*-isomer **12c** and the characteristic CO band maximum in IR occurred[16] at a lower frequency for the *trans*-isomer **12d**.

UV and IR spectra of some of the cyclopropane compounds described are given in Table 3, and these show similarities with those of the *trans*-acid **12d**.

The high stereoselectivity in the cyclopropane formation may be rationalised from the stereoselectivity observed in related reactions for the preparation of other cyclopropane derivatives.[14,15,17]

As lactonic ester **10** could be a possible intermediate for this novel cyclopropane formation, it was heated with dry sodium ethoxide in benzene. This provided a 1:1 mixture of the cyclopropyl carboxylic acid **4d** and the *trans*-lactone **6a**.

Stereoelectronic assistance in the cyclisation of the stabilised carbanion (A) (Scheme 1) to form the cyclopropane compound would be sterically unfavourable[18] when the ester CO and the large phenyl group are *cis* to each other in the transition state, and this probably

Table 2. ^{1}H-NMR signal for cyclopropyl methyl

Compound	τ($CDCl_3$)
4a	9.21
4b	9.18
4c	9.12
4d	9.05
4e	9.12
4g	8.80
4h	8.83
4j	8.98
12a[14]	9.03
12b[14]	8.60

Table 1.

Lactones	Stereochemistry	Signals for the hydrogen attached to alkoxy-carbon (τ)	Multiplet centred at (τ)
6f	*trans*	5.22–5.54	5.38
11b	*cis*	5.02–5.30	5.16
6b	*trans*	5.30–5.64	5.47
11a	*cis*	4.80–5.00	4.90
6c	*trans*	5.90–6.30	6.10
11c	*cis*	5.02–5.37	5.19

Table 3. UV and IR spectra of some cyclopropane compounds

Compounds	λ_{max}nm(ε)	ν_{max}(cm^{-1})
4d	227(7586)	1681
	268(468)	
4e	224(10,000)	
	267(476)	
4l	224(8511)	1677
	268(517)	
4n	—	1680
4g	—	1684
4i	—	1688
12d[15]	222(11,000)	1688
	267(380)	
12c[15]	219(7500)	1694
	261(200)	

explains the high stereoselectivity of the cyclisation process.

In a highly nonpolar solvent like benzene, attack of the ethoxide ion on the carbonyl C of the lactone is the main path to the cyclopropyl derivatives. In the case of lactonic esters having *peri*-substituents (from epoxides **2a** and **2b**), this path (Path a) is the exclusive one as no lactonic product could be detected. In the case of the lactonic esters formed from the epoxides **2(e–f)**, the conformational factor, and the flexible nature of the 7-membered ring are probably responsible for the attack of the ethoxide ion only on the ester CO resulting in the formation of normal products, i.e. the *trans*-lactones **6(b–c)**. Lactones are the only products of ring-opening of all epoxides when heated under reflux in ethanol.

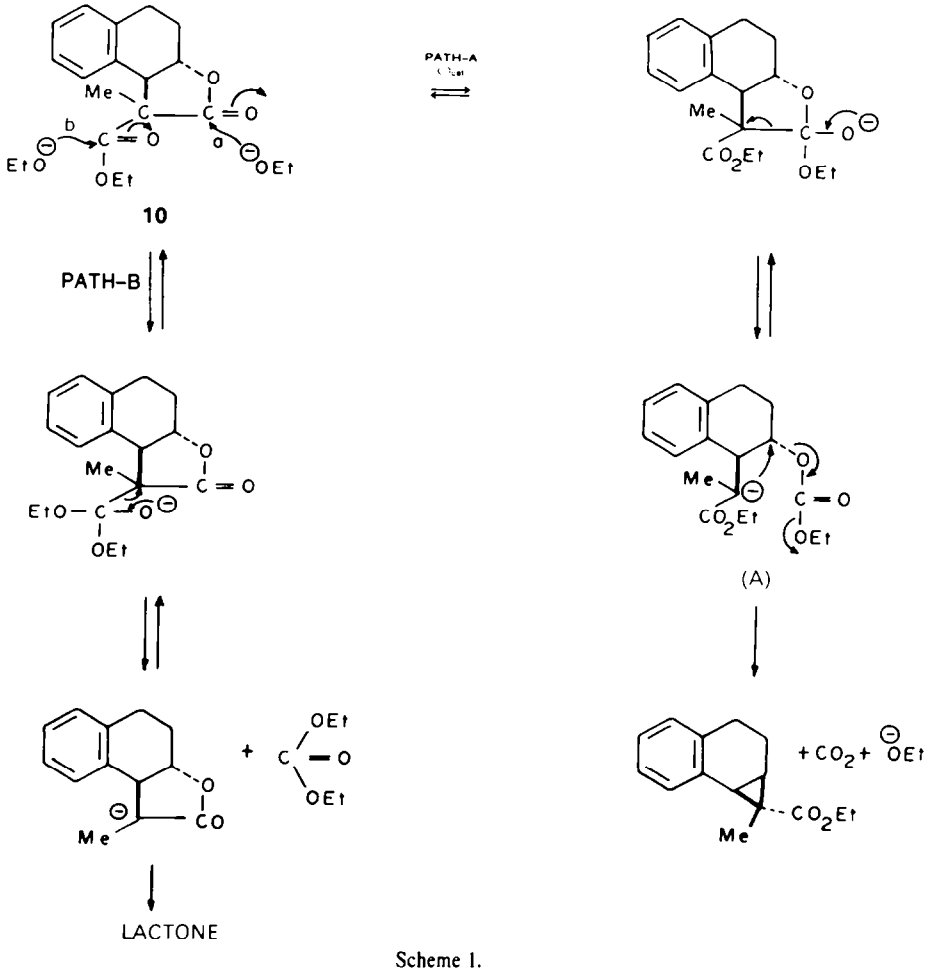
In a medium of very low dielectric constant, such as benzene, the ethoxide ion exists essentially as ion-pairs or higher aggregates, and the attack of this bulkier anion on the more sterically accessible carbonyl C of the lactone is, therefore, the most favoured path.†

The lactone formation step being reversible (Scheme 1), the epoxides **2e** and **2f**, which failed to give cyclopropane were heated under reflux with the carbanion in benzene in presence of some diethyl carbonate. The epoxide **2e** only under these conditions afforded in low yield the desired crystalline cyclopropane derivative **4i**.

REGIOSPECIFIC CLEAVAGE OF THE CYCLOPROPANE CARBOXYLIC ACIDS

Different types of cyclopropyl derivatives, conjugated with the CO or phenyl group, have been cleaved regioselectively with metal in liquid ammonia and the mechanisms have been discussed.[19] One important factor

†The nature of the metal cation associated with the ethoxide ion may also play an important role, and this has not been investigated.



Scheme 1.

which controls the direction of ring-opening, is the ability of the CO or phenyl group to overlap with an adjacent cyclopropyl bond. When there are two modes of cleavage possible, stabilisation of the intermediate radical ion has been found to be the deciding factor. Dreiding molecular models of the carboxylic acids reported in this paper suggest that the external a, b bond overlaps better with the π-system of the benzene ring, and this accounts for the regiospecific cleavage observed for the cyclopropyl carboxylic acids with Na in liquid ammonia. Each cyclopropyl acid afforded initially a diastereomeric mixture of the acid **13**. Repeated fractional crystallisations in each case provided a pure isomer. The pure acids obtained through Na–liquid ammonia cleavage of **4b** and **4d** were found to be identical respectively with the acids **14a** and **14b** reported[1] from our laboratory.

In the catalytic hydrogenolysis of substituted cyclopropane, the direction of ring-opening is governed[20] by the electronic nature of substituents; and hydrogenolysis is much faster[20] at Pd than at Pt. Pd–C was used to study the mode of cleavage of several cyclopropane derivatives.[21] We were therefore interested to study catalytic cleavage of the cyclopropane carboxylic acids such as **4d** and **4g** using Pd–C. In each case a diastereomeric mixture of the cleavage products **13c** and **13d** as mentioned before was isolated.

EXPERIMENTAL

The compounds described are racemic. The same experimental procedures and instruments were used as described[1] previously. In addition some spectral measurements were performed on a Varian T-60 NMR spectrometer. EtOH used was dried over Mg and liquid ammonia was used directly from the tank.

trans - 4 - *Bromo* - 5 - *hydroxyhomochroman* **7c**. A soln of **8a**[8] (1.75 g) in DMSO (52 ml) and water (0.5 g) was treated with NBS (4.24 g) under N_2 as prescribed.[9] This afforded **7c** (2.12 g, 72%) as shining colourless cubes, m.p. 84–85°; ν_{max} 3578 cm^{-1}. (Found: C, 49.20; H, 4.78. $C_{10}H_{11}O_2Br$ requires: C, 49.41; H, 4.56%.)

4,5-*Epoxyhomochroman* **2e**. To an ice-cold stirred soln of **7c** (2.5 g) in abs EtOH (40 ml) was added dropwise during 20 min a soln of KOH (985 mg) in dry MeOH (9.85 ml). The stirring in the cold was continued for 1 hr. Work-up as described[3] afforded **2e** (1.3 g, 78%), b.p. 90–95° (bath)/0.3 mm. (Found: C, 73.87; H, 6.32. $C_{10}H_{10}O_2$ requires: C, 74.06; H, 6.21%).

trans - 1,2 - *Benzo* - 4 - *bromo* - 3 - *hydroxycyclohept* - 1 - *ene* **7d**. A soln of **8b**[10] (1.6 g) in DMSO and H_2O was treated with NBS to afford *trans*-**7d** (2.23 g, 83%) as shining colourless crystals, m.p. 89–91°; τ 2.33–3.47 (4H, m), 5.07 (1H, d, J 8 Hz), 5.54–5.93 (1H, m) and 7.07–8.73 (7H, m). (Found: C, 54.58; H, 5.34. $C_{11}H_{13}OBr$ requires: C, 54.78; H, 5.39%.)

3,4 - *Epoxy* - 1,2 - *benzocyclohept* - 1 - *ene* **2f**. **7b** (2.5 g) on treatment with methanolic-KOH afforded **2f** as a colourless oil (1.6 g), b.p. 105–110° (bath)/2 mm (reported[22] b.p. 80°/0.04 mm).

2 - *Methyl* - 3,4 - *dihydronaphthalene* - 1,2 - *oxide* **9**. An ice-cold soln of 2 - methyl - 3,4 - dihydronaphthalene[23] (1.36 g) in ether (10 ml) was treated with permonophthalic acid (1.39 g) in ether (63 ml). After 66 hr at 0°, the mixture yielded **9** (1.07 g, 71%), b.p. 75–85° (bath)/1.5 mm; m.p. 53–56°; τ 2.70–3.00 (4H, m) 6.40 (1H, s), 7.00–8.34 (4H, m) and 8.45 (3H, s). (Found: C, 82.65; H, 7.54. $C_{11}H_{12}O$ requires: C, 82.46; H, 7.55%.)

6 - *Methoxy* - 7 - *methyl* - 1a,2,3,7b - *tetrahydro* - 1 - *ethoxycarbonyl* - 1 - *methylcyclopropa*[*a*]*naphthalene* **4a**, *and the corresponding carboxylic acid* **4b**

(a) *Heating in benzene under a typical procedure.* To a stirred soln of sodium diethyl methylmalonate, prepared from Na–dust (300 mg, 0.01 g atom) and diethyl methylmalonate (1.8 g, 0.01 mole) in dry benzene (20 ml), was added dropwise under N_2 a soln of **2a** (1 g, 0.005 mole) in dry benzene (8 ml) and heated under reflux for 6–7 hr. After complete addition, the salt went into soln and the stirring heating was continued for further 30 hr. The mixture was then cooled and poured into ice-water (200 ml). The product was extracted with ether (3 × 50 ml), and the combined extracts washed with water, dried and evaporated. The resulting oily material was distilled under vacuum to afford the following fractions: (i) unchanged **2a** (350 mg), b.p. 100°/0.3 mm; (ii) the ester **4a** (420 mg, 30%), b.p. 140°/0.3 mm; ν_{max} 1718 cm^{-1} and (iii) an oil (0.2 g), b.p. 150°/0.3 mm; ν_{max} 1712 and 1722 cm^{-1}. The fraction (ii) was redistilled to provide an analytical sample of **4a**, b.p. 120° (bath)/0.3 mm; ν_{max} 1711 cm^{-1}; τ 3.35 (2H, q, aromatic protons), 5.84 (2H, q, J 6.8 Hz, $O\underline{CH_2}Me$), 6.22 (3H, s, OMe), 7.00–7.85 (5H, m, $2CH_2$ and one cyclopropyl proton), 7.96 (3H, s, aromatic $\underline{Me}$), 8.73 (3H, t, J 6.80 Hz), 9.21 (3H, s, cyclopropyl CH_3), and one cyclopropyl proton is lost in the Me signal of the ester. (Found: C, 74.21; H, 8.08. $C_{17}H_{22}O_3$ requires: C, 74.42; H, 7.86%.)

The aqueous alkaline soln after separation of the neutral product was acidified with HCl and the liberated acid was extracted with ether. Usual processing of the extract gave **5a**[3] (450 mg, 32%), m.p. 152–153° (ether–light petroleum).

The above **4a** (350 mg) was hydrolysed by heating under reflux for 1 hr with a soln of NaOH (560 mg) in EtOH (112 ml) and H_2O (28 ml). Alcohol was removed under reduced pressure, the residue was diluted with ice-water, and the neutral material, if any, was removed by extraction with ether. The alkaline soln on acidification, and subsequent extraction with ether (2 × 75 ml) furnished **4b** (200 mg, 60%), m.p. 199–201°. Recrystallisation provided pure **4b**, m.p. 200–201° (Et_2O-light petroleum); λ_{max} 209 (ϵ19,950) and 280 nm (ϵ2045); ν_{max} 1684 cm^{-1}. This acid is sparingly soluble in aq. $NaHCO_3$ and 2% NaOH. (Found: C, 73.40; H, 7.38. $C_{15}H_{18}O_3$ requires: C, 73.15; H, 7.37%.)

The neutral ester fraction (iii) on similar alkaline hydrolysis afforded an acid which was heated at 140° for 25 min. The resulting brown oil was dissolved in ether. Usual processing of the solvent afforded an additional amount of the acid **4b** (120 mg); m.p. 197–201°.

In one experiment, when the above condensation was performed by heating for 15 hr, the major product was **2a**, and the yield of the desired ester **4a** was much reduced (15%).

The acid **4b** (60 mg) was esterified with CH_2N_2 to furnish the methyl ester (45 mg), b.p. 125–130° (bath)/0.1 mm, ν_{max} 1712 cm^{-1}; τ 9.18 (cyclopropyl Me).

(b) *Heating under reflux in DME.* The condensation of **2a** with the carbanion afforded two fractions: (i) a semisolid material (530 mg), ν_{max} 1720 cm^{-1} and (ii) a residue (350 mg) showing weak lactone C=O and ester C=O in IR. Fraction (i) (530 mg) was hydrolysed with dil base as before to give the crystalline acid **4b** (280 mg), m.p. 200°. Fraction (ii) (350 mg) similarly furnished the same acid **4b** (200 mg), m.p. 200°.

7 - *Bromo* - 6 - *methoxy* - 5 - *methyl* - 1a,2,3,7b - *tetrahydro* - 1 - *methyl* - *cyclopropa*[*a*]*naphthalene* - 1 - *carboxylic acid* **4c**. Interaction of **2b**[3] (4.05 g) with sodioenolate of diethyl methylmalonate afforded a highly viscous oil (3.96 g), b.p. 145–175°/0.2 mm; ν_{max} 1710 cm^{-1}. Hydrolysis of this material with methanolic KOH (40 ml, 5%) provided an oily acid (3.1 g). Crystallisation of this material provided pure **4c** (1.6 g), m.p. 182–184° (Et_2O-light petroleum); ν_{max} 1682 cm^{-1}; τ 0.54 (1H, s), 3.13 (1H, s), 6.22 (3H, s), 6.83–7.55 (4H, m), 7.72 (3H, s), 8.28–9.00 (2H, m) and 9.12 (3H, s). (Found: C, 55.77; H, 5.19. $C_{15}H_{17}O_3Br$ requires: C, 55.38; H, 5.23%.)

The mother liquors from the above crystallisations afforded an oil (1 g), ν_{max} 1711 cm^{-1}. Chromatography of this material over silica gel (40 g) and elution with ether–light petroleum (5 : 95) gave an additional amount of **4c** (180 mg), m.p. 182–184°. Thus the total yield of **4c** was (1.78 g, 37% on the basis of epoxide **2b** used).

1a,2,3,7b - *Tetrahydro* - 1 - *methyl* - *cyclopropa*[*a*]*naphthalene*-1 - *carboxylic acid* **4d**; *and* α - 1 - (1,2,3,4 - *tetrahydronaphthol*-2) - *propionic acid lactone* (trans) **6a**. Reaction of **2c**[3,5] (3.4 g) with diethyl methylmalonate anion in benzene gave a viscous oil (3.65 g), b.p. 120–124°/0.3 mm. Trituration of this material with light petroleum furnished the *trans*-**6a** (250 mg) as needles, m.p. 152–153° (Et_2O–light petroleum) (reported[6] m.p. 152–153°); ν_{max} (KBr) 1775 cm^{-1}; τ 2.47–2.86 (4H, m), 5.66–6.15 (1H, m), 6.63–

8.22 (6H, m) and 8.37 (3H, d, J 7.10 Hz). (Found: C, 77.09; H, 7.11. $C_{13}H_{14}O_2$ requires: C, 77.20; H, 6.98%.)

The above petroleum ether on concentration furnished an oily material (3 g, 60%), ν_{max} (film) 1719 cm^{-1}. Hydrolysis of this product with dil base afforded **4d** (2.2 g, 47% on the basis of **2c**), m.p. 131–132° (Et_2O–light petroleum); ν_{max} (Nujol) 1681 cm^{-1}; λ_{max} 227 (ϵ7586) and 268 nm (ϵ4677); τ 1.53 (1H, s), 2.56–2.93 (4H, m), 6.77–8.71 (6H, m) and 9.05 (3H, s). (Found: C, 77.17; H, 7.18; N.E. 203.3. $C_{13}H_{14}O$ requires: C, 77.20; H, 6.98%; N.E. 202.3.)

The aqueous alkaline soln, after separation of the neutral product provided an additional amount (100 mg) of **6a**; and thus the total yield of the lactone was (350 mg, 7.5%).

Methyl-1a,2,3,7b - *tetrahydro* - 1 - *methyl* - *cyclopropa[a]naphthalene* - 1 - *carboxylate* **4e**. **4d** (1.56) was esterified with CH_2N_2 to give **4e** (1.4 g, 83%), b.p. 118° (bath)/0.2 mm; λ_{max} 224 (ϵ10,040) and 267 nm (ϵ480); ν_{max} 1720 cm^{-1}; τ 2.53–2.93 (4H, m), 6.25 (3H, s), 6.76–8.70 (6H, m) and 9.12 (3H, s); m/e 216(M^+), 201(M^+–Me), 185(M^+–OMe), 184(M^+–MeOH) and 157(M^+–CO_2Me). (Found: C, 77.71; H, 7.36. $C_{14}H_{16}O_2$ requires: C, 77.75; H, 7.46%.)

trans - 2 - *Hydroxy* - 1,2,3,4 - *tetrahydro* - 1 - *naphthyl* - α - *propionic acid* **5b**. The *trans*-**6a** (216 mg) was hydrolysed by heating under reflux for 4 hr with methanolic KOH (4 ml, 7%). Usual work-up afforded the *trans*-**5b** (220 mg), m.p. 108° (Et_2O–light petroleum); ν_{max} 1705 cm^{-1}. (Found: C, 70.63; H, 7.35. $C_{13}H_{16}O_3$ requires: C, 70.89; H, 7.32%.)

This acid **5b** (70 mg) on distillation at 145–150° (bath)/0.2 mm gave the *trans*-**6a** as needles (63 mg), m.p. 152–153°.

(gem - *Ethoxycarbonyl* - *methyl*)*cyclopropa[c]chroman* **4f**. Interaction of **2d**[7] (1.90 g) with the anion of diethyl methylmalonate as before afforded **4f** as a viscous oil (1.9 g, 64% based on epoxide **2d**), b.p. 125–130°/0.3 mm; ν_{max} 1705 cm^{-1} (Found: C, 72.52; H, 7.30. $C_{14}H_{16}O_3$ requires: C, 72.39; H, 6.9%.)

(gem - *Carboxy* - *methyl*) *cyclopropa[c]chroman* **4g**. **4f** (1.90 g) was hydrolysed by heating under reflux for 2 hr with methanolic KOH (63 ml, 2%). Usual work-up and purification of the acid by extraction with aq. $NaHCO_3$ provided the pure **4g** (1.45 g, 87%) m.p. 125–126° (Et_2O–light petroleum), ν_{max} 1684 cm^{-1}; τ 0.04 (1H, s), 2.67–3.33 (4H, m), 5.66 (2H, d, J 2.90 Hz), 7.21 (1H, d, J 10 Hz), 7.52–7.82 (1H, m) and 8.80 (3H, s). (Found: C, 70.36; H. 5.92; N.E. 204.1. $C_{12}H_{12}O_3$ requires: C, 70.58; H, 5.92; N.E. 204.2.)

(gem - *Methoxycarbonyl* - *methyl*) *cyclopropa[c]chroman* **4h**. **4g** (880 mg) was esterified with CH_2N_2 to furnish **4h** (900 mg, 96%), m.p. 47–50° (light petroleum; b.p. 40–60°); ν_{max} 1709 cm^{-1}; τ 2.72–3.33 (4H, m), 5.69 (2H, d, J 3 Hz), 6.30 (3H, s), 7.34 (1H, d, J 10 Hz), 7.66–7.93 (1H, m) and 8.83 (3H, s); m/e 218(M^+), 203(M^+–Me), 186(M^+–MeOH), and 159(M^+–CO_2Me). (Found: C, 71.29; H, 6.68. $C_{13}H_{14}O_3$ requires: C, 71.54; H, 6.47%.)

α - (trans - 4 - *Hydroxy* - 5 - *homochromanyl*) *propionic acid lactone* **6b**; *and* (gem - *carboxy* - *methyl*) *cyclopropa[d]homochroman* **4i**. Sodioenolate of diethyl methylmalonate was prepared from Na-dust (770 mg) and diethyl methylmalonate (5.7 ml) in dry benzene (36 ml). To this mixture was then added diethyl carbonate (5 ml). A soln of **2e** (2.88 g) in dry benzene (5 ml) was added to the refluxing mixture as before. Usual work-up gave a neutral product as an oily solid (3.64 g). Trituration of this material with ether furnished the *trans*-**6b** (1.9 g), m.p. 132–133° (acetone–light petroleum); ν_{max} 1770 cm^{-1}; τ 2.60–3.10 (4H, m), 5.30–5.64 (1H, m), 5.64–8.28 (6H, m) and 8.61 (3H, d, J 6.6 Hz). (Found: C, 71.37; H, 6.65. $C_{13}H_{14}O_3$ requires: C, 71.54; H, 6.47%.)

The ether soln after separation of **6b** on evaporation gave a semisolid (1.7 g), ν_{max} 1760 (w) and 1710 cm^{-1} (s). This material was hydrolysed by heating under reflux for 5 hr with methanolic KOH (35 ml, 7%). The acidic material (900 mg) thus obtained was heated at 165° for 25 min. The residue on usual separation afforded a neutral product, i.e. **6b** (300 mg), and an acidic material (392 mg, 10% based on epoxide **2e**), ν_{max} 1690(s) cm^{-1}. Esterification of this acid with CH_2N_2 provided **4j** (380 mg), b.p. 85–95° (bath)/0.1 mm; ν_{max} 1710 cm^{-1} (s); m/e 232(M^+), 200(M^+–MeOH), 173(M^+–CO_2Me) and 145(M^+–CO_2Me–CH_2=CH_2); τ 2.99–3.33 (4H, m), 5.67–6.10 (2H, m), 6.35 (3H, s), 7.17–7.50 (1H, m), 7.87–8.17 (2H, m), 8.67–8.90 (1H, m) and 8.98 (3H, s).

Ester **4j** (380 mg) was hydrolysed by methanolic KOH (12 ml, 2%). Usual work-up gave pure **4i** (315 mg), m.p. 111–112° (Et_2O–light petroleum); ν_{max} 1685 cm^{-1}. (Found: C, 71.18; H, 6.55. $C_{13}H_{14}O_3$ requires: C, 71.54; H, 6.47%.)

Treatment of the aqueous alkaline soln from the above condensation afforded an additional amount of the *trans*-**6b** (400 mg). Thus **6b** (2.6 g, 64%) was the predominant product, and **4i** (392 mg, 10%) was the minor one.

Similar condensation of **2e** with the carbanion in the absence of diethyl carbonate provided mainly *trans*-**6b** (63%) and **4i** only in 5% yield.

α - (trans - 4 - *Hydroxy* - 1,2 - *benzocyclohepten* - 3 - *yl*) *propionic acid lactone* **6c**. Interaction of **2f** (3.8 g) with the carbanion in benzene afforded only *trans*-**6c** (3.19 g, 62%), m.p. 128–129° (Et_2O–light petroleum); ν_{max} 1764 cm^{-1}; τ 2.65–2.90 (4H, m), 5.90–6.30 (1H, m), 6.62–8.45 (8H, m) and 8.53 (3H, d, J 6 Hz). (Found: C, 77.42; H, 7.61. $C_{14}H_{16}O_2$ requires: C, 77.75; H, 7.46%.)

Condensation of sodium diethyl methylmalonate with trans-2-*bromo* - 1,2,3,4 - *tetrahydronaphthalene* - 1 - *ol* **7a** *and formation of* α - *carbethoxy* - α - 1 - (1,2,3,4 - *tetrahydronaphthol* - 2) *propionic acid lactone* (trans) **10**, *and the* trans-*lactone* **6a**. To a stirred and refluxing soln of the anion of diethyl methylmalonate, prepared from diethyl methylmalonate (4.2 g) and Na-dust (550 mg) in dry benzene, (25 ml) was added dropwise during 6 hr under N_2 a soln of **7a**[3] (2.7 g) in dry benzene (20 ml). After stirring and refluxing for 8 hr more, the mixture yielded an oily solid (1.94 g), b.p. 130–135°/0.2 mm. This material on trituration with light petroleum afforded the *trans*-**6a** (950 mg, 40%) as needles, m.p. 151–152°.

The above petroleum ether soln on evaporation furnished the **10** (980 mg, 31%) as oil, b.p. 165° (bath)/0.2 mm; ν_{max} 1725 and 1775 cm^{-1}; τ 2.6–3.14 (4H, m), 4.96–5.45 (1H, m), 5.54–5.90 (2H, *q*, *J* 7 Hz), 6.58–8.09 (5H, m) and 8.16 and 8.48 (two sharp singlets accounting for 3 protons), 8.53–9.02 (3H, two overlapping triplets accounting for 3 protons, J 7.1 Hz). (Found: C, 70.21; H, 6.94. $C_{16}H_{18}O_4$ requires: C, 70.06; H, 6.61%.)

Condensation of sodium diethyl methylmalonate with trans - 3 -*bromo* - 4 - *hydroxychroman* **7b** *under refluxing benzene*. The interaction of **7b**[7] with the carbanion furnished only *trans*-**6f**, and a hydroxy-ester which on alkaline hydrolysis afforded a pure isomer of **5c**. The spectral properties of **6f** and **5c** will be presented later in detail as these are the products of ring opening of epoxide **2d** with the carbanion under refluxing EtOH.

Condensation of diethyl sodio iso*propylmalonate with the epoxide* **2c**; *formation of ethyl* 1a,2,3,7b-*tetrahydro*-1-iso-*propyl* -*cyclopropa[a] naphthalene* - 1 - *carboxylate* **4k**, *the corresponding carboxylic acid* **4l**, *and* α - iso*propyl* - 1 - (1,2,3,4 - *tetrahydronaphthol* -2) *acetic acid lactone* (trans) **6d**. The interaction of **2c** (4 g) with sodium diethyl *iso*propylmalonate yielded (i) a light yellow oil (2.01 g), b.p. 130–135°/0.1 mm; ν_{max} 1702 (s) and 1771 (w) cm^{-1}; (ii) a viscous oil (1.34 g), b.p. 145–175°/0.2 mm; ν_{max} 1737 (m) and 1777 (s) cm^{-1}.

Fraction (i) (2.01 g) was hydrolysed by heating under reflux for 2 hr with methanolic KOH (71 ml, 2%) and afforded a neutral (1.27 g), and acidic products (380 mg), m.p. 152–155°. Recrystallisation of this acid gave 1a,2,3,7b - *tetrahydro* - 1 iso*propyl* - *cyclopropa[a]naphthalene* - 1 - *carboxylic acid* **4l**, m.p. 158–159°: λ_{max} 224 (ϵ8511) and 268 nm (ϵ517); ν_{max} 1677 cm^{-1}; τ −0.48 (1H, s), 2.68–3.07 (4H, m), 7.02–7.54 (3H, m), 7.60–8.75 (4H, m) and 8.97 (6H, d, J 4.2 Hz). (Found: C, 78.13; H, 8.02. $C_{15}H_{18}O_2$ requires: C, 78.23; H, 7.88%.)

The neutral product (1.27 g) was distilled to give **4k** (1.25 g), b.p. 115–120° (bath)/0.2 mm; λ_{max} 224 (ϵ8128) and 268 nm (ϵ447); ν_{max} 1710 cm^{-1}. (Found: C, 78.37; H, 8.69. $C_{17}H_{22}O_2$ requires: C, 79.03; H, 8.58%.)

The ester **4k** (1.25 g) was hydrolysed by heating for 1.5 hr with powdered Kt-BuO (3.7 g) in DMSO (36 ml). Acidification of the resulting alkaline soln and subsequent ether extraction provided the acid **4l** (1.05 g), m.p. 157–159°; ν_{max} 1677 cm^{-1}.

Fraction (ii) (1.34 g) was hydrolysed by heating under reflux for 1 hr with a soln of NaOH (2.68 g) in EtOH (176 ml) and H_2O

(132 ml). This afforded **4k** (400 mg), ν-max 1705 cm^{-1}, and an oily acidic material (700 mg). This acid was heated at 170–175° for 25 min to furnish a semisolid neutral product (460 mg). Chromatography of this material over silica gel (17 g) and elution of the chromatogram with Et_2O–light petroleum (5:95) afforded the *trans*-**6d** (210 mg, 3.5%), m.p. 92–94° (Et_2O–light petroleum); ν_{max} 1781 cm^{-1}; τ 2.80 (4H, m), 5.80–6.34 (1H, m), 6.72–8.36 (7H, m) and 8.65–8.90 (6H, two doublets overlapping J 7.2 Hz). (Found: C, 78.03; H, 7.72. $C_{15}H_{18}O_2$ requires: C, 78.23; H, 7.88%). The total yield of the cyclopropyl acid **4l** was 1.6 g (26%) and that of *trans*-**6d** (210 mg, 35%) on the basis of **2c** used.

Methyl 1a,2,3,7b - *tetrahydro* - 1 - *isopropyl* - *cyclopropa[a]naphthalene* - 1 - *carboxylate* **4m**. **4l** (300 mg) was esterified with diazomethane to furnish **4m** (250 mg), m.p. 68–70° (petroleum ether, b.p. 40–60°); λ_{max} 225 (ϵ6607) and 268 nm (ϵ398); ν_{max} 1710 cm^{-1}; τ 2.74–2.90 (4H, m), 6.27 (3H, s), 6.85–7.51 (3H, m), 7.58–8.73 (4H, m) and 8.95 (6H, d, J 4.5 Hz); *m/e* 244(M^+), 212(M^+–MeOH), 201(M^+–$CHMe_2$) and 185(M^+–CO_2Me). (Found: C, 78.65; H, 8.32. $C_{16}H_{20}O_2$ requires: C, 78.65; H, 8.25%.)

Interaction of sodium diethyl isopropylmalonate *with* 3,4 - *epoxychroman* **2d**; *formation of* gem - *carboxy* - isopropyl) *cyclopropa[c]chroman* **4n**; α-(trans - 3 - *hydroxy* - 4 - *chromanyl*) - β - *methylbutyric acid lactone* **6e** and α - (trans - 3 - *hydroxy* - 4 - *chromanyl*) - β - *methylbutyric acid* **5e**. Condensation of **2d** (2.5 g) with *iso*propylmalonate anion furnished: (i) a light yellow viscous oil (700 mg), b.p. 127–140°; ν_{max} 1778 (v,w.) and 1716 cm^{-1}(s); (ii) a yellow viscous oil (1.1 g), b.p. 145–155°/0.4 mm; ν_{max} 1778 (v.w.) and 1716 cm^{-1}(s); and (iii) a highly viscous oil (670 mg), b.p. 180–185°(bath)/0.4 mm; ν_{max} 1778(m) and 1715 cm^{-1}(s).

Fraction (i) (700 mg) on alkaline hydrolysis with methanolic KOH (21 ml, 2%) furnished a neutral product (360 mg), ν_{max} 1708 cm^{-1}, and an oily acid (330 mg), ν_{max} 1705 cm^{-1}. This (360 mg) was hydrolysed with Kt.BuO in DMSO to furnish a crude acid (300 mg), m.p. 188–190°. Recrystallisation of this acid afforded pure **4n**, m.p. 196–198° (Et_2O–light petroleum); ν_{max} 1680 cm^{-1}; τ 1.00 (1H, s), 2.66–3.33 (4H, m), 5.60 (2H, d, J 4 Hz), 7.19 (1H, d, J 10 Hz), 7.53–7.83 (1H, m), 8.07–8.60 (1H, m), 8.77 (3H, d, J 5.4 Hz) and 9.07 (3H, d, J 6 Hz). (Found: C, 71.92; H, 7.01. $C_{14}H_{16}O_3$ requires: C, 72.39; H, 6.94%.). Mother liquors of the above crystallisations provided an oily acid A. (110 mg) which was chromatographed (see later). The oily acid (330 mg) obtained after alkaline hydrolysis of fraction (i) was heated at 170–175° for 25 min to furnish a neutral product as red oil (180 mg), ν_{max} 1776 cm^{-1}(m) and 1709 cm^{-1}; and an oily acid B (120 mg) which was chromatographed later.

Alkaline hydrolysis of fraction (ii) (1.1 g) afforded a neutral product as an oil (200 mg), and an oily acid (900 mg), 1703 cm^{-1}. Hydrolysis of the above neutral material (200 mg) with KtBuO in DMSO furnished an additional amount of **4n** (70 mg). Mother liquors of the crystallisations afforded an oil C (60 mg) which was chromatographed. The acidic product (900 mg) obtained from alkaline hydrolysis of fraction (ii) was heated at 170–175° for 25 min to furnish a semisolid neutral material (400 mg), and an acidic material D (300 mg) which was chromatographed. The above neutral product (400 mg) was chromatographed over silica gel (16 g). Elution of the chromatogram with Et_2O–light petroleum (5:95) gave the *trans*-**6e** (110 mg), m.p. 116–118° (ether–light petroleum); ν_{max} 1785 cm^{-1}; τ 2.60–3.33 (4H, m) 5.20–5.60(m), 5.60–6.33 (2H, m), 6.33–8.33 (3H, m) and 8.65–8.85 (6H, two doublets overlapping, J 6 Hz). (Found: C, 72.22; H, 7.06. $C_{14}H_{16}O_3$ requires: C, 72.39; H, 6.94%.)

The above acidic materials A–D (600 mg) were chromatographed over silica gel (20 g). Elution of the chromatogram with ether–light petroleum (5:95) afforded an additional amount of **4n** (95 mg), m.p. 196–198°. Ether–light petroleum (20:80) eluted the *trans*-**5e** (50 mg), m.p. 168–170° (Ether–light petroleum), ν_{max} 1700 cm^{-1}. (Found: C, 67.40; H, 7.22. $C_{14}H_{18}O_4$ requires: C, 67.18; H, 7.25%.)

Fraction (iii) (670 mg) afforded the pure **6e** (50 mg), and **5e** (100 mg).

The aqueous alkaline soln. after separation of the neutral product was acidified to give an oily acid (800 mg). This on heating at 160–175° afforded an additional amount of the **6e** (105 mg), m.p. 115–116°.

The total yield of **4n** was (365 mg, 9%), the *trans*-**5c** (150 mg, 3.6%), and *trans*-**6e** (260 mg, 6.6%) on the basis of **2d** used.

(gem - Isopropyl - *methoxycarbonyl*) cyclopropa[c] chroman **4o**. **4n** (80 mg) was esterified with CH_2N_2 to give a crude methyl ester (90 mg), m.p. 75–84°. Recrystallisation provided pure ester **4o** (68 mg, 80%), m.p. 85–87° (light petroleum, b.p. 40–60°), ν_{max} 1710 cm^{-1}. (Found: C, 72.92; H, 7.12. $C_{15}H_{18}O_3$ requires: C, 73.15; H, 7.37%.)

Alkaline hydrolysis of the lactone **6e**; *formation of* α - (trans - 3 - *hydroxy* - 4 - *chromanyl*) - β - *methylbutyric acid* **5e**. The *trans*-**6e** (100 mg) was hydrolysed by heating under reflux for 5 hr with methanolic KOH (1.4 ml, 7%). This provided the pure *trans*-**5e** (100 mg, quantitative), m.p. 168–170° (Et_2O–light petroleum).

Lactonisation of the trans - *hydroxy* - *acid* **5e**. **5e** (110 mg), m.p. 168–170° was heated in an oil bath maintained at 170–175° for 20 min. The resulting residue on sublimation at 130–160° (bath)/0.2 mm afforded a mixture of pure *trans*-**6e** (42 mg, 40%), m.p. 116–118° (Et_2O–light petroleum), and unchanged **5e** (50 mg, 45%), m.p. 168–170° (Et_2O–light petroleum).

Condensation of epoxide and bromohydrin in ethanol

Ethyl - α - (trans - 3 - *hydroxy* - 4 - *chromanyl*)*propionate* **5d**. To an ice-cold soln of NaOEt, prepared from Na-metal (0.97 g, 0.04 g.atom) in Mg-dried EtOH (42 ml) was added under N_2 diethyl methylmalonate (7.3 g, 0.04 mole). To this stirred and refluxing soln of the resulting enolate, was added dropwise a soln of **2d** (3.15 g, 0.02 mole) in EtOH (30 ml). After heating under reflux for 7 hr more, the mixture was cooled, diluted with water, and the product was extracted with ether (3 × 100 ml). The combined extract was washed with water, dried, and evaporated. The residue thus obtained was fractionated to furnish a diastereomeric mixture of **5d** (4.03 g, 76%), b.p. 140–145°/0.15 mm; ν_{max} 3572 and 1721 cm^{-1}. (Found: C, 66.95; H, 7.10. $C_{14}H_{18}O_4$ requires: C, 67.18; H, 7.25%.)

α - (trans - 3 - *Hydroxy* - 4 - *chromanyl*)*propionic acid lactone* **6f**, *and a pure isomer of* α - (trans - 3 - *hydroxy* - 4 - *chromanyl*)*propionic acid* **5c**. **5d** (4.0 g) was hydrolysed by heating under reflux for 2 hr with methanolic KOH (56 ml, 3%). This afforded an oily acid (3.8 g). This acid was heated at 160° for 25 min, and the residue provided a neutral solid product (980 mg), and an acid as a viscous oil (2.4 g). The neutral material (980 mg) on recrystallisations furnished the pure **6f** (680 mg), m.p. 118–119° (Et_2O–light petroleum); ν_{max} 1785 cm^{-1}; τ 2.64–3.33 (4H, m), 5.22–5.54 (1H, m), 5.54–6.07 (2H, m), 6.75–7.53 (2H, m) and 8.42 (3H, d, J 6 Hz). TLC showed a single spot using MeOH–benzene (20:80) as the eluting solvent. (Found: C, 70.64; H, 6.10. $C_{12}H_{12}O_3$ requires: C, 70.58; H, 5.92%.)

The oily acid (2.4 g) on trituration with Et_2O–light petroleum provided a solid which on repeated recrystallisations furnished a pure isomer of *trans*- **5c** (970 mg, 27%), m.p. 147–149° (Et_2O–light petroleum), ν_{max} 1710 cm^{-1}. (Found: C, 64.74; H, 6.60. $C_{12}H_{14}O_4$ requires: C, 64.85; H, 6.35%.) Mother liquors after separation of the pure isomer, afforded an oily acid which on heating at 160° for 15 min and subsequent sublimation of the residue at 150° (bath)/0.2 mm furnished an oily solid which on crystallisations provided an additional amount of *trans*- **6f** (500 mg), m.p. 118–119°. The overall yield of the pure lactone **6f** was (1.18 g, 36% based on **2d**).

Lactonisation of the pure isomer of the trans - *hydroxy* - *acid* **5c**; *formation of a pure isomer of* α - (trans - 3 - *hydroxy* - 4 - *chromanyl*)*propionic acid lactone* **6g**; *and the recovered hydroxy-acid* **5c**. The pure isomer of **5c** (600 mg), m.p. 147–149° was heated at 160° for 15 min, and the residue was distilled at 145–165° (bath)/0.2 mm to afford a solid product as a mixture. Usual separation with base furnished a neutral product characterised as the *trans*-**6g** (180 mg, 32%), m.p. 116–117° (Et_2O–light petroleum), m.m.p. with the isomeric *trans*-lactone **6f** was 105–114; ν_{max} 1789 cm^{-1}; τ 2.77–3.25 (4H, m), 5.23–5.50 1H, m), 5.50–6.00 (2H, m), 6.40–7.12 (2H, m) and 8.73 (3H, d, J 7.2 Hz). TLC as before proved its homogeneous nature. (Found: C, 70.58; H, 5.81. $C_{12}H_{12}O_3$ requires: C, 70.58; H, 5.92%.)

The above alkaline extract provided the unchanged pure isomer of **5c** (200 mg, 33% recovery), m.p. 147–149°.

Alkaline hydrolysis of the lactones **6(f–g)**; *formation of a pure isomer of the* trans - *hydroxy* - *acid* **5c**. **6f** (250 mg), m.p. 118–119° was hydrolysed with methanolic KOH (4.2 ml, 7%) and afforded an oily acid (250 mg) which provided a pure sample of the **5c** (91 mg), m.p. 147–149° mentioned above.

Similar hydrolysis of the isomeric lactone **6g** (90 mg) furnished the pure *trans*-**5c** (70 mg), m.p. 147–149°.

Treatment of the trans-*lactone* **6f** *with potassium carbonate in refluxing xylene.* The lactone **6f** (250 mg), m.p. 118–119° was heated under reflux for 24 hr with freshly baked K_2CO_3 (300 mg) under dry xylene (7.5 ml). Usual work-up afforded a solid which on recrystallisation furnished the unchanged **6f** (180 mg, 72%), m.p. 118–119°.

Isomerisation of the trans-*lactone* **6g**. **6g** (150 mg) on refluxing with K_2CO_3 in dry xylene initially afforded an oily solid (150 mg). Fractional crystallisations provided a pure sample of the isomeric *trans*-**6f** (50 mg, 33%), m.p. and m.m.p. 118–119°.

Mother liquors of the above crystallisations afforded a mixture of **6(f–g)**, m.p. 95–105° as evidenced from its ^{1}H-NMR spectrum, two characteristic doublets for the Me groups at τ 8.39 (J 6 Hz) and 8.70 (J 7.8 Hz) indicated it to be a 10:7 mixture of **6f** and **6g** respectively. (Found: C, 70.72; H, 6.03%.)

α - (trans - 4 - *Hydroxy* - 5 - *homochromanyl*)*propionic acid lactone* **6b** Heating *trans*-**7c** (1.5 g, 0.006 mole) with the anion of diethyl methylmalonate (0.012 mole) in ethanol initially provided a solid product (1.24 g), m.p. 125–130°; ν_{max} 1786(s) and 1740 cm^{-1}(w). Alkaline hydrolysis of this material with methanolic KOH (7%) afforded an acid which on heating at 160–170° furnished the previously mentioned *trans*-**6b** (860 mg, 64% based on **7c**), m.p. 132–133° (acetone–light petroleum).

Attempted alkaline hydrolysis of **6b** with base followed by careful acidification gave back the lactone **6b**.

α - (trans - 4 - *Hydroxy* - 1,2 - *benzocyclohepten* - 3 - *yl*) *propionic acid lactone* **6c**. Similar condensation of the *trans*-**7d** (4 g) furnished a light viscous oil (3 g), b.p. 155–165°/0.2 mm; ν_{max} 1772(s) and 1728(m) cm^{-1}. This material on hydrolysis with dil base followed by acidification afforded the previously reported crystalline **6c** (2.48 g, 69%), m. p. 128–129°.

Attempted alkaline hydrolysis of **6c** and acidification gave back **6c**.

Hydrogenolysis of cyclopropane carboxylic acids—α - (1,2,3,4 - *Tetrahydro* - 2 - *naphthyl*)*propionic acid* **13c**

(a) *By Na–liquid ammonia reduction of* **4d**. To well-stirred undistilled liquid ammonia (200 ml) was added a small piece of Na–metal (one-third of the total amount used). To the resulting blue-coloured soln was added in a slow stream a soln of **4d** (200 mg, 0.001 mole) in dry Et_2O (25 ml). The remainder of the Na–metal (total Na used, 92 mg, 0.004 g atom) was then added. The blue-coloured soln was stirred for 20 min and then solid NH_4Cl was added in small portions to discharge the blue colour. After evaporation of ammonia at r.t., the residue was diluted with water, and acidified with cold conc. HCl. The liberated acid was extracted with ether (3 × 75 ml) and the extract was washed with H_2O, dried and evaporated. The crude solid acid (200 mg), m.p. 70–85°; ν_{max} 1710 cm^{-1} thus obtained on repeated recrystallisations furnished a pure isomer (13 mg), m.p. 116–117° (light petroleum) and this was found to be identical in all respects with the stereoisomer **14b** reported[1] from our laboratory. (Found: C, 76.51; H, 8.15. $C_{13}H_{16}O_2$ requires: C, 76.44; H, 7.90%.)

Mother liquors of the above crystallisations affroded an isomeric mixture of **13c**, m.p. 72–85° which was further recrystallised to give an analytical sample as a mixture, m.p. 78–95°; τ0.28 (1H, s), 2.74–2.90 (4H, m), 6.92–8.56 (8H, m) and 8.73 (3H, d, J 6.8 Hz). (Found: C, 76.33; H, 8.16%.). Attempted separation of another isomer through chromatography was not rewarding.

(b) *By catalytic hydrogenolysis of* **4d**. A soln of **4d** (500 mg) in EtOH (15 ml) was hydrogenated over Pd–C (100 mg, 10%) at NTP. After absorption of theoretical quantity of H_2 the catalyst was filtered off, and the solvent was removed under reduced pressure. The acid residue was purified through aq $NaHCO_3$ to furnish a mixture of acids (380 mg, 72%), m.p. 65–101°. Repeated recrystallisations afforded the pure isomer **14b**, m.p. 116–117°; ν_{max} 1705 cm^{-1}. (Found: C, 76.45; H, 8.03%.)

Mother liquors of the above crystallisations afforded a diastereoisomeric mixture of **13c**, m.p. 108–114°; ν_{max} 1704 cm^{-1}. (Found: C, 76.50; H, 8.05%.)

7 - *Methoxy* - 8 - *methyl* - α - (1,2,3,4 - *tetrahydro* - 2 - *naphthyl*)*propionic acid* **13a**. Reduction of **4b** (75 mg) with Na–metal in liquid ammonia afforded **13a** (67 mg) as a mixture. Recrystallisations provided a pure **14a**, m.p. 128–129° (Et_2O–light petroleum); m.m.p. with an authentic sample[1] was undepressed. (Found: C, 72.52; H, 8.28. $C_{15}H_{20}O_3$ requires: C, 72.55; H, 8.12%.)

7 - *Methoxy* - 6 - *methyl* - α - (1,2,3,4 - *tetrahydro* - 2 - *naphthyl*)*propionic acid* **13b**. A soln of **4c** (300 mg) was reduced with Na–metal in liquid ammonia to furnish **13b** (220 mg) as a mixture, m.p. 108–112°. Repeated recrystallisations afforded a pure **13b**, m.p. 125–126° (Et_2O–light petroleum); ν_{max} 1704 cm^{-1}; τ 3.12 (1H, s), 3.43 (1H, s), 6.22 (3H, s), 7.13–7.5 (4H, m), 7.83 (3H, s), 7.88–8.58 (4H, m), and 8.74 (3H, d, J 6.5 Hz). (Found: C, 72.90; H, 8.47. $C_{15}H_{20}O_3$ requires: C, 72.55; H, 8.12%.)

α - (3 - *Chromanyl*)*propionic acid* **13d**

(a) *By* Na–*liquid ammonia reduction.* Reduction of **4g** (300 mg) with Na–metal in liquid ammonia furnished **13d** (300 mg) as a mixture, m.p. 114–142°; ν_{max} 1705 cm^{-1}. Repeated recrystallisation of this acid furnished a pure isomer of **13d** (60 mg), m.p. 153–154° (Et_2O–light petroleum), ν_{max} 1711 cm^{-1}; τ −0.51 (1H, s), 2.69–3.34 (4H, m), 5.52–6.29 (2H, m), 7.10–7.66 (4H, m) and 8.71 (3H, d, J 6 Hz). (Found: C, 70.22; H, 6.83. $C_{12}H_{14}O_3$ requires: C, 69.89; H, 6.84%.)

Mother liquors of the above crystallisations provided a mixture, m.p. 118–130°, ν_{max} 1704 cm^{-1}; τ 2.70–3.32 (4*H, m*), 5.57–6.13 (2H, m), 7.07–7.66 (4H, m) and 8.71 (3H, d, J 6 Hz). (Found: C, 70.18; H, 6.75%.)

(b) *By catalytic hydrogenolysis of* **4g**. An ethanolic soln of **4g** (150 mg) was hydrogenolysed over Pd–C (10%) to give an isomeric mixture of **13d** (150 mg), m.p. 110–120°; ν_{max} 1704 cm^{-1}. Repeated recrystallisations of this mixture as before finally provided a pure isomer of **13d**, m.p. 153–154° mentioned above.

Mother liquors of the above crystallisations afforded a diastereomeric mixture of **13d**, m.p. 115–125°; ν_{max} 1704 cm^{-1}; τ −0.20 (1H, s), 2.87–3.44 (4H, m), 5.54–6.33 (2H, m), 6.87–8.20 (4H, m) and 8.71 (3H, d, J 6 Hz). (Found: C, 69.72; H, 7.07%.)

α - Iso*propyl* - α - (1,2,3,4 - *tetrahydro* - 2 - *naphthyl*)*acetic acid* **13e**. Na-liquid ammonia reduction of the **4l** (300 mg) afforded **13e** (300 mg) as a mixture, m.p. 80–91°. Repeated recrystallisations of this mixture furnished a pure isomer of **13e**, m.p. 103–104° (light petroleum); ν_{max} 1703 cm^{-1}; τ 2.79–3.00 (4H, m); 7.03–7.37 (4H, m), 7.63–8.35 (6H, m) and 8.97 (6H, d, J 6.1 Hz). (Found: C, 77.60; H, 8.13. $C_{15}H_{20}O_2$ requires: C, 77.55; H, 8.68%.)

α - (3 - *Chromanyl*) - β - *methylbutyric acid* **13f**. Reduction of the acid **4n** (220 mg) with Na–liquid ammonia afforded **13f** (220 mg); as a mixture, m.p. 60–80°. Repeated recrystallisation provided a pure isomer of **13f**, m.p. 101–102° (light petroleum, b.p. 40–60°); ν_{max} 1703 cm^{-1}. (Found: C, 71.65; H, 7.58. $C_{14}H_{18}O_3$ requires: C, 71.77; H, 7.74%.)

Mother liquors of the above crystallisations furnished **13f** as a diastereomeric mixture, m.p. 60–80°; τ −0.22 (1H, s), 2.80–3.33 (4H, m), 5.50–6.67 (2H, m), 7.00–8.40 (5H, m) and 8.94 (6H, d, J 5.5 Hz). (Found: C, 72.04; H, 7.5%.)

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