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BASE CATALYSED REARRANGEMENT OF OXYCOPE SYSTEMS[1]

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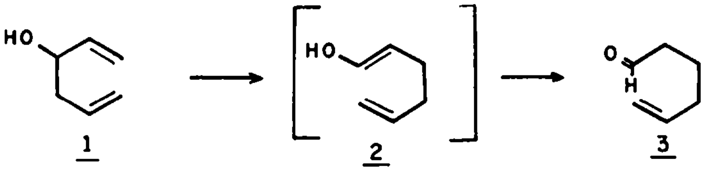
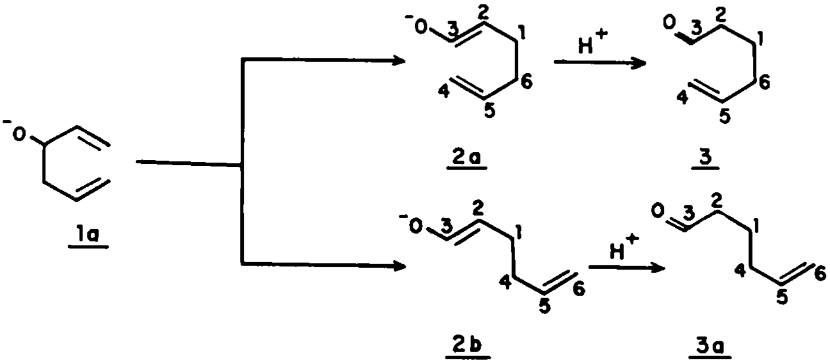
Abstract - The synthesis and rearrangements of the chiral carbinols 8 and 9 are described. With KH-THF, both the carbinols gave optically active rearrangement products; with alkali in methanol, they gave optically inactive rearrangement products. The results are interpreted as favouring a concerted mechanism for the hydride catalysed rearrangements and a non-concerted mechanism for the rearrangements catalysed by alkali in methanol.

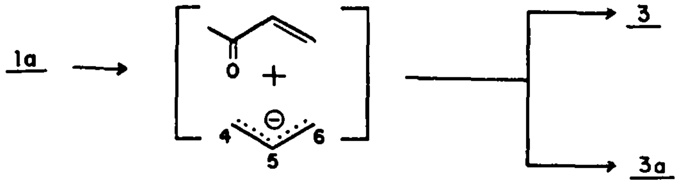
An oxy-Cope system is a 3-hydroxy-1,5-hexadiene system of the type 1. When heated, it rearranges to a carbonyl compound of the type 3 via the enol 2.



Relatively high temperatures (>200°C) are required for this rearrangement named by Berson[2] as an oxyCope rearrangement. A variation of this process in basic media would involve the corresponding anion 1a whose rearrangement would give the enolate 2a which after protonation gives a carbonyl compound of the type 3. Because of enolate formation this process is faster than the rearrangement of the neutral substrate 1. In the presence of a base, the enolate 1a may also rearrange to the enolate 2b which after protonation can give carbonyl compounds of the type 3a, after protonation. The above rearrangements may be concerted in which case the rearrangement of 1a to 3 is a (3,3) sigmatropic rearrangement also referred to as an anionic oxyCope rearrangement whereas the rearrangement of 1a to 3a is a (1,3) sigmatropic rearrangement. The end products 3 and 3a will be different if the system 1 is suitably substituted.

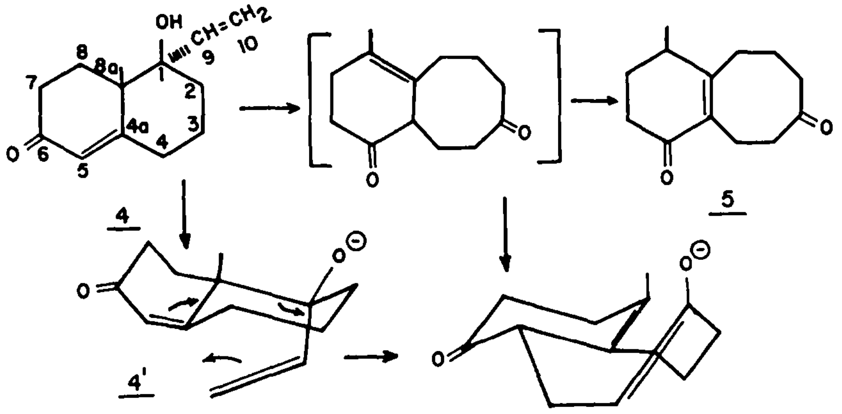


The rearrangement of 1a to 3 or 3a may also involve a fragmentation-recombination mechanism as follows :

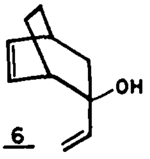


Products 3 and 3a will result depending on whether the Michael addition takes place at C_4 or C_6.

The anionic oxyCope process was first[3] invoked by us as a possible mechanism for the base catalysed rearrangement of the vinyl carbinol 4 to the diketone 5 - the same product as obtained by refluxing the carbinol 4 in diethylene glycol.



The carbon atoms C_{10}, C_9, C_1, C_{8a}, C_{4a} and C_5 with an -OH at C_1 constitute the oxy-Cope moiety in carbinol 4. This mechanism is better visualized in the conformation 4' where C_{10} and C_5 are within bonding distance. The same rearrangement was observed with many oxyCope substrates of the type 4 - which contain a carbonyl group conjugated with the terminal olefinic carbon atom away from the anionic centre. In our earlier studies we favoured a fragmentation - recombination mechanism (retroaldol followed by Michael addition) to rationalise such rearrangements. Later, with other substratesof the type 6 and 7 Evans and coworkers[4] established that they undergo rearrangements through a concerted mechanism.



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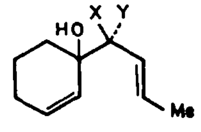
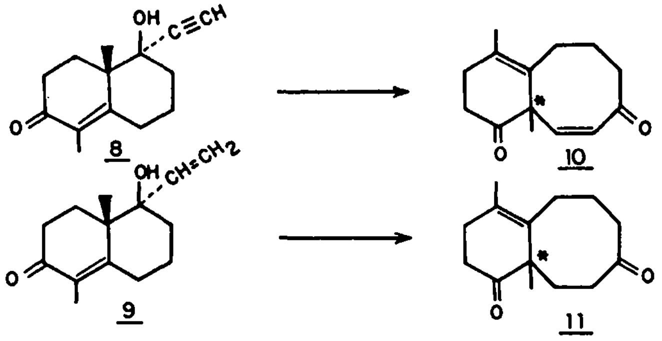
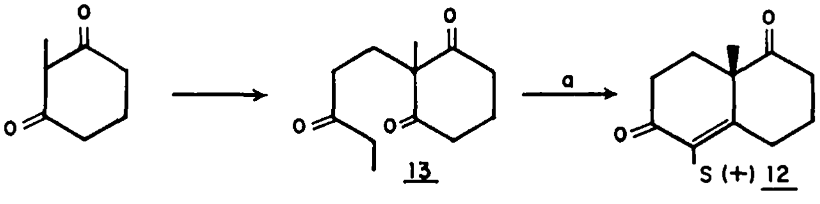


X = H ; Y = OMe
Y = H ; X = OMe 7

In a preliminary communication[5] we reported the synthesis and rearrangement of the optically active ethynyl and vinyl carbinols 8 and 9. These rearrangements were found to be concerted when carried out with KH-THF and non-concerted with KOH-MeOH. We wish to report herein the full details of these studies.



The rationale for the choice of chiral systems 8 and 9 as substrates is that on rearrangement a chiral centre is created at the ring junction with simultaneous loss of existing chiral centres and that the products should be optically active or racemic depending on whether rearrangement occurs in a concerted or non-concerted manner respectively. The obvious starting material for the synthesis of the chiral carbinols 8 and 9 is the optically active dione 12. This chiral dione has been obtained by Yamada *et al*[6] by asymmetric cyclization, of the triketone 13 in the presence of (s)-proline pyrrolidide in 50% chemical and 60% optical yield. The trione 13 is accessible by Michael addition of ethylvinylketone to 2-methyl-1,3-cyclohexane dione.



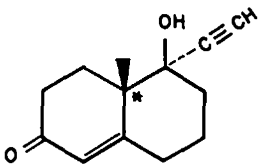
a = S-Prolinepyrrolidide

We preferred to use the easily accessible 1-chloro-3-pentanone to alkylate 2-methyl-1,3-cyclohexanedione. This alkylation was carried out in refluxing ethyl acetate in the presence of an excess of triethylamine to give the trione 13, in 75% yield. Yamada's procedure gave us mixture of optically active dione 12 and uncyclized trione 13. The use of (S)-proline or (S)-alanine in the presence of catalytic amounts of perchloric acid found successful for similar cyclizations to the diones of the type 12 gave high chemical yields of 12 but with low optical purity. However, when the asymmetric cyclization of trione 13 was carried out in acetic acid at 120° in the presence of (S)-phenylalanine[7], dione (+)12 was obtained as a pale yellow liquid in 80% chemical and 85% optical yield. The optical purity of this diketone was estimated both from its specific rotation and also from the splitting of the vinyl-CH$_3$ group in the PMR spectrum taken in the presence of

Eu (hfc)$_3$. The 8aS configuration assigned for this compound by Yamada et al is well supported by its CD spectrum which is similar to that of 8aS Wieland-Mischer ketone.

Synthesis of the chiral carbinols 8 and 9

The dione S(+)12 when treated with lithium acetylide/ammonia furnished the optically active carbinol 8 as a colourless crystalline solid m.p.174-176° in 40% yield. $[\alpha]_D^{25}$ + 79.9° ($CHCl_3$), with expected spectral data. The 1-β-hydroxy-1-α-ethnyl configuration was assigned on analogy to the course of ethynylation observed for similar systems[8].



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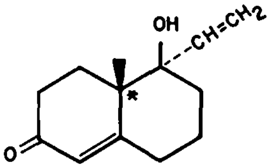
(IR,8aS)



15
(IR,8aS)

Partial hydrogenation of carbinol 8 (Pd/$CaCO_3$) in pyridine furnished the vinyl carbinol 9 as a colourless crystalline solid m.p. 90-91°. $[\alpha]_D^{25}$ + 178°($CHCl_3$) with expected spectral absorptions. The C.D. curves of carbinols 8 and 9 were similar to those of the carbinols 14 and 15 and hence they were assigned 1R, 8aS configuration.

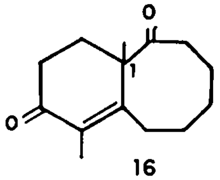
Rearrangement of the chiral carbinol 8

We have previously reported[9] the rearrangement of carbinol dl-8 to the ring enlarged racemic dione 10 by treatment with NaOMe/MeOH. Similar treatment of the chiral carbinol 8 gave after work up and purification the same dione 10 with zero rotation. However, treatment of the same carbinol with KH/THF furnished a crystalline solid mp. 64.5-65.5° in 65-70% yield based on recovered starting material, $[\alpha]_D^{25}$ + 335° ($CHCl_3$). Mass spectrum, analysis and spectral absorptions confirmed the product to be the chiral dione 10. The rearrangement of the optically active ethynyl carbinol (8) to optically active dione 10 could be effected also by treatment with potassium methoxide in THF though in reduced chemical and optical yields (20% and 90-95% respectively).

Rearrangement of chiral carbinol 9

The racemic carbinol 9 has been found by us[9] earlier to rearrange to the racemic dione 11 when treated with KOH/MeOH. The chiral carbinol 9 also gave the same dione 11 with zero rotation when refluxed with KOH/MeOH. However treatment with KH/THF under conditions similar to those described for chiral carbinol 8 furnished after chromatography over alumina two products each in 30% chemical yield. The first compound eluted with 20% ethyl acetate-hexane was obtained as a colourless solid m.p. 55-57° $[\alpha]_D^{25}$ + 20.2° ($CHCl_3$). The I.R. showed unconjugated C=O absorption whereas PMR showed an olefinic -CH_3 and a quaternary CH_3. The mass spectra and elemental analysis showed the product to be isomeric with the starting material. It was obvious that this product was the chiral dione 11.

The second compound eluted with 40% ethyl acetate-hexane was a viscous liquid (homogeneous on TLC) $[\alpha]_D^{25}$ + 24° ($CHCl_3$). IR showed conjugated and unconjugated C=O absorptions while PMR showed an olefinic $-CH_3$ and an angular methyl. The mass spectrum and elemental analysis showed it to be isomeric with the starting material. These data are consistent with either of the structures 16 or 17 for the above liquid product.



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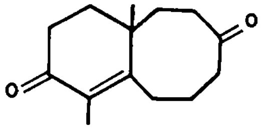
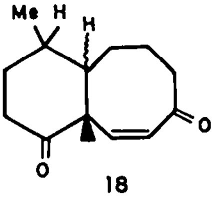


17

The proton decoupled ^{13}C NMR of this compound showed the following features : 21.5 (s, $>C=O$), 200 (s, $>C=O$), 164.2 (s, vinyl carbon), 136.8 (s, vinyl carbon), 44.5 (t, CH_2), 42.5 (t, CH_2), 42 (s, quaternary carbon), 37.2 (t, CH_2), triplets for four methylenes at 36.6, 34, 32.2 and 29, 28.8 (q, vinyl-CH_3), 14.4 (q, angular CH_3). These data strongly support structure 17. In structure 16, C_1 is flanked by a C=O on the one hand and a π bond on the other hand and may be expected to appear at a lower field compared to all the other methylene carbons. Since this peak appears at higher field (42 ppm) as compared to the methylene carbons at 44.5 and 42.5, structure 16 may be ruled out.

The comparatively low specific rotation observed for dione 11 as compared to that of dione 10 suggested that perhaps the rearrangement of carbinol 9 to dione 11 involved partial racemization. This possibility was however ruled out when catalytic reduction of chiral dione 10 with PtO_2 furnished dione 11 with identical specific rotation. It is interesting to note here that the hydrogenation of chiral carbinol 10 with Pd-C in ethyl acetate at room temperature resulted surprisingly in the reduction of the tetrasubstituted double bond to furnish an isomeric enedione 18, m.p. 100-2° $[\alpha]_D^{25}$+ 25.8° ($CHCl_3$). While the stereochemistry of this reduction is uncertain, the IR and PMR absorptions confirm the gross structure 18.



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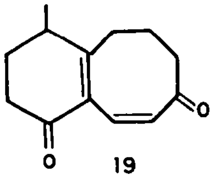

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Whereas the compounds 18 and 19 show^{3a} well-defined AB quartets for the vinyl protons, the same protons show up as a singlet in compound 10. This is probably due to some conformational feature of the molecule resulting in accidental equivalence of the two vinyl protons. The splitting of these protons could however be observed in the presence of Eu(hfc)$_3$

Mechanism of the rearrangements and stereochemistry of the products

Since the use of bases like KOH or NaOMe in a hydroxylic solvent like methanol gave rearrangement products with no rotation, it is reasonable to assume that the rearrangements proceed by a fragmentation-recombination mechanism as in Chart I.

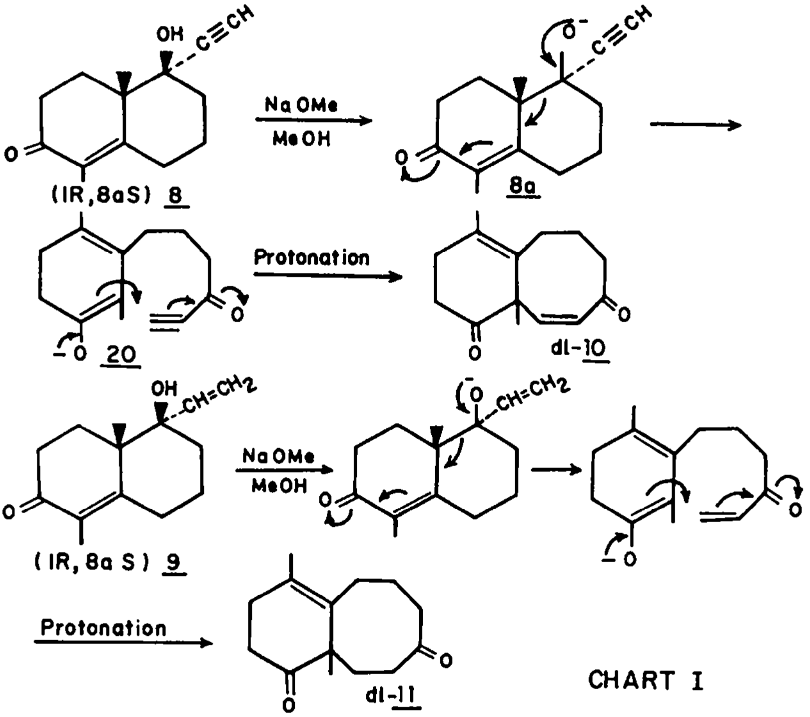

CHART I

An alternative mechanism is to assume that the enolate 20 is in reversible equilibrium with the racemic species 8a, 8b and 21 which are then transformed to the racemic dione 10 by concerted processes (Chart-II)

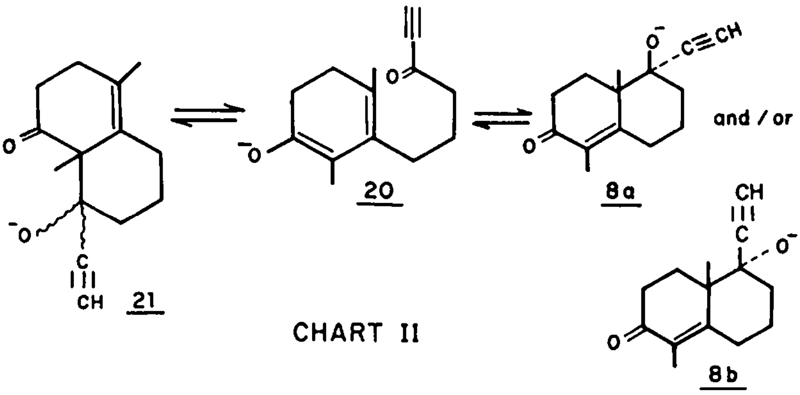

CHART II

Since, however the starting carbinol 8 was recovered in 40 % yield with little loss of optical activity and with no evidence of formation of the racemic carbinols corresponding to the species 8a, 8b and 21, this second mechanism must be ruled out. In view of the experimental fact that chiral dione 10 results by treatment even with KOMe in tetrahydrofurane, a third explanation for the formation of racemic diones 10 and 11 would be to assume that the reactions first give optically active products which undergo racemization subsequently. This possibility was soon discounted since chiral dione 10 could be recovered unaffected in optical purity and other respects after treatment with KOMe/MeOH.

On the otherhand, the retention of optical activity in the products obtained by treatment with KH in THF is strong evidence for the operation of a concerted mechanism. The fact that the chiral rearrangement products 10 & 11 were obtained as sharp melting solids and that chiral dione 10 could be hydrogenated to chiral dione 11 in excellent optical and chemical yields indicate that these compounds were optically pure. This was confirmed when studies with $Eu(hfc)_3$ showed no splitting of either of the two methyl groups in optically active 10, though they shifted to lower fields as expected with increasing concentration of the shift reagent. The formation of the optically active compound 17 may be rationalized as arising from a 1,3-sigmatropic rearrangement. These transformations are depicted in Chart III.

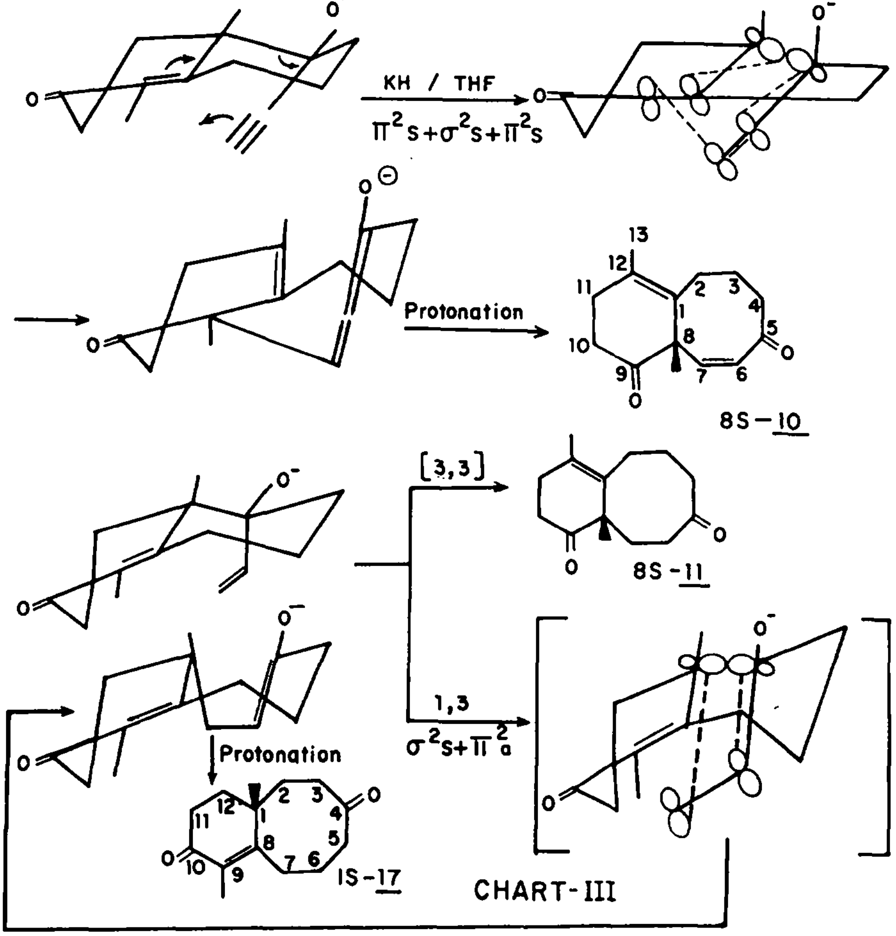

CHART-III

The transition state for the rearrangement in KH/THF though polar must be quite tight, facilitating maximum transfer of chirality. In a polar medium (KOMe/MeOH) this transition state must be less tight due to increased polarity and may be expected to lead to loss of chirality.

In view of the fact that (3,3)sigmatropic rearrangements occur most commonly in a suprafacial manner with respect to both the π systems, the resulting methyl group in 10 (and also 11) may be expected to have β-orientation. Based on priority rules[10], this carbon must then have a 'S' configuration in both the diones 10 and 11.

As for the configuration of the chiral C_1 in 17, it is probably 1S with the same configuration as C_{8a} in the starting carbinol 9 since the transition state for a $\sigma^2s + \pi^2a$ migration must be more favourable than for a $\sigma^2a + \pi^2s$ migration. Also, the same transition state must be energetically more favoured than those involved in the 1,3 shift leading to the isomer 16.

To sum up, the present study has demonstrated the dual nature of the mechanism of rearrangements[11] of bicyclic oxyCope substrate of the type 8 and 9.

Experimental

All melting points and boiling points are uncorrected. Infra-red spectra were recorded using a Perkin Elmer 598 instrument. PMR spectra were taken using Varian EM-390 and XL-100 instruments with $CDCl_3$ and CCl_4 as solvents. Tetramethyl silane (TMS) was used as the internal standard. The chemical shifts are reported in the δ -scale. The PMR chemical shifts of doublets and multiplets reported do not correspond to the calculated chemical shifts, but represent the δ -values corresponding to the centre of the multiplets. Mass spectra were recorded using a varian Match-7 Mass spectrometer. The optical rotations were measured using a Billingham and Stanley polarimeter (model D). CD curves were recorded using Model J.20 CD instrument. TLC was run over glass plates coated with silica gel-G (ACME) (0.25 mm thickness) and visualised using iodine. Anhydrous sodium sulphate was used as the drying agent. Hexane refers to petrol boiling between (60°- 80°); petroleum ether refers to (40°- 60°) boilingfraction.

2-Methyl-2-(3'-oxopentyl)-1,3-cyclohexanedione 13

Procedure A

Potassium metal (10 g, 0.25 g.atom) was dissolved in dry methanol (110 ml) diluted with dry ether (250 ml), 2-methyl-1,3-cyclohexanedione (30 g, 0.24 mole) was added and the mixture was stirred for 30 min. Methanol and ether were removed by distillation and dry DMF (50 ml) was added. The chloroketone (30 g, 0.24 mole) in dry DMF (50 ml) was added with stirring and the reaction mixture was allowed to stand overnight. The separated potassium chloride was filtered and DMF was removed in vacuo. The residue was taken up in ether, washed with water and dried. The residue after removal of ether was distilled to get the triketone 1g (b.p. 126-128°/0.5 mm (reported[11] b.p.129-131°/mm).Yield 25 g (49.6%).

Procedure B

To a mixture of 2-methyl-1,3-cyclohexanedione (10g, 0.08 mole) in dry ethyl acetate (100 ml) and triethyl amine (50 ml, in 100 ml dry ethyl acetate) was added 1-chloro-3-pentanone (11 g, 0.08 mole) and mixture refluxed for 15hr. The separated triethylamine hydrochloride was filtered and washed with dry ethyl acetate. The combined filtrate was distilled under reduced pressure to remove ethyl acetate and excess triethyl amine. The residue was taken up in chloroform washed with dil. HCl followed by water. Chloroform was removed after drying by distillation to afford a brown liquid which was chromatographed on silica gel. Elution with 10% ethyl acetate-hexane furnished the triketone as a pale yellow liquid, b.p.129-131°/1 mm.

Yield 12.6 g (75%). IR($CHCl_3$) λ max 1715 cm^{-1} (C=O), 1695 cm^{-1} (C=O) PMR(CCl_4/TMS) δ values 1.0(t, 3H, $COCH_2\underline{CH_3}$), 1.22 (s, 3H, ang-CH_3), 1.6-2.9 (m, 12H, methylenes).

Asymmetric cyclization of 2-methyl-2-(3'-oxopentyl)-1,3-cyclohexanedione 13

This cyclization was studied under different reaction conditions using different α-amino acids. The results are summarized in Table I.

Table 1
Asymmetric cyclization of triketone 13 to dione S(+) 12

Triketone 13	Amino acid & additive	Solvent (ml)	Temp°C	Time	Chemical yield of 12	Optical yield of 12
1) .01 m	S-proline (.005 m) 1N $HClO_4$ (3 ml)	CH_3CN (30)	80	18 h	74%	15%
2) .01 m	S-proline (.01 m)	HOAc (20)	30	12 h	Mixture of starting material and aldols	
3) .01 m	S-proline (.005 m) 1N HCl (a few drops)	CH_3CN (20)	80	6 h	Only starting material	
4) .01 m	S-proline (.01 m) HOAc (a few drops)	,,	80	12 h	Mixture of starting material & aldols	
5) .01 m	S-Alanine (.01 m) 1N $HClO_4$ (3 ml)	,,	80	20 h	20%	20%
6) .01 m	S-phenylalanine (.01 m) 1N $HClO_4$ (3 ml)	,,	80	20 h	20%	15%
7) .01 m	S-phenylalanine (.01 m) HOAc (a few drops)	,,	80	6 h	mostly starting material	
8) .01 m	,, (.01 m)	HOAc (20)	30	20 h	mixture of starting material & aldols	
9) .05 m	S-Phenylalanine (.05 m)	HOAc(100)	120	2 h	80%	85%

The best procedure (entry 9 in Table I) for synthesis of S(+)-1,2,3,4,6,7,8,8a-octahydro-5,8a-dimethyl-1,6-naphthalene dione (S-12) is as follows :

To the triketone 13 (10.5 g, 0.05 mole) dissolved in freshly distilled acetic acid (100 ml) was added (S)-phenyl alanine (8.25 g, 0.05 mole) in portions and the mixture was heated at 120° (bath temperature) with stirring for 2 hr. Acetic acid was removed by distillation under reduced pressure. The residual material was taken up in chloroform and filtered to recover the chiral amino acid almost quantitatively. The filtrate was washed successively with dil.$NaHCO_3$ solution, water and dried. Removal of chloroform by distillation furnished a brown viscous liquid which was chromatographed over silica gel. Elution with 10% ethyl acetate-hexane gave the diketone 12 as a pale yellow viscous liquid: b.p. 125-130°/0.5 mm (Reported[6] b.p. 145-150°/3 mm). Chemical yield - 7.6 g (80%). Optical yield - 85% $[\alpha]_D^{25}$ + 69° (C = 0.017, MeOH) Reported[6] $[\alpha]_D^{25}$ + 79° for 100% pure enantiomer. IR($CHCl_3$) λmax (cm^{-1}), 1710 (C=O), 1665 (unsatd. C=O), 1610 (C=C). PMR ($CDCl_3$/TMS) δ values : 1.4 (s, 3H, ang-CH_3), 1.8 (s, 3H, vinyl CH_3), 1.8-3.0 (m, 10H, methylenes). CD(Dioxan) λ (nm) : 290, 242, 220 $[\theta]$obs : +0.0036, -0.0064, +0.012. The CD data were similar to those[12] of Wieland-Miecher ketone.

(1R, 8aS) (+)1-α-ethynyl-1-β-hydroxy-6-oxo-5,8a-dimethyl-1,2,3,4,6,7,8,8a-octahydronaphthalene 8

In a 1 lt 3 necked flask fitted with a gas inlet tube dropping funnel, mercury sealed stirrer and an outlet, distilled NH_3 (500 ml) was collected. Lithium metal (1.8 g of lithium, 0.25 g atom) was added slowly in portions and converted into the acetylide by bubbling dry acetylene. After the complete conversion of lithium into lithium acetylide, the flask was cooled to -70°C (liquid N_2 - ethyl acetate bath) and a solution of the diketone 12 (19.2 g, 0.1 mole) in dry ether (30 ml) was added with vigorous stirring during 10 min. Stirring at -70° was continued for another 3.5 hr while maintaining a slow stream of acetylene through the reaction mixture and the rosy-red mixture was decomposed with solid NH_4Cl (15 g). Most of the ammonia and ether were evaporated during 1 hr by taking the reaction mixture in a wide mouthed crystallizing trough. Water was then added to the residue and the precipitated ethynyl carbinol was filtered, washed with water and dried. The crude material on crystallization from a mixture of chloroform-hexane gave the optically active ethynyl carbinol 8 as a colourless crystalline solid. m.p. 174-176°. Yield - 8.7 g (40%). $[\alpha]_D^{25}$ + 79.9° (C = 0.0267, $CHCl_3$). UV λ_{max}^{MeOH} 250 nm (ϵ = 13734). IR (KBr) λmax (cm^{-1}): 3380 (-OH), 3260(-C≡C-H), 2110 (-C≡C-) 1645 (conjugated -C=O), 1610 (C=C). PMR ($CDCl_3$/TMS) δ values : 1.25 (s, 3H, ang CH_3), 1.8 (s, 3H, vinyl CH_3), 1.85-2.7 (m, 12H, methylenes, C≡CH, -OH). CD(C = 0.495, Dioxan) λ nm : 321, 240, 210 Δ E : -1.51, + 6.53, + 6.015. These CD data are similar to those of carbinol 14 given below : λ nm 320-330 230, 208. $[\theta]$ obs : -0.0057, +0.016, + 6.018. Analysis $C_{14}H_{18}O_2$ requires : C = 77.06, H = 8.2%, Found : C = 77.25, H = 8.22%

(1R, 8aS) (+)1α-vinyl-1β-hydroxy-6-oxo-5,8a-dimethyl-1,2,3,4,6,7,8,8a-octahydronaphthalene 9

A solution of the ethynyl carbinol 8 (2.18 g, 0.01 mole) in dry pyridine (15 ml) was hydrogenated in the presence of 5% Pd-$CaCO_3$ (0.2 g) at 50 psi for 20 min. The catalyst was filtered and washed with ether. The filtrate was concentrated under reduced pressure and the residue was taken up in ether. The ether solution was washed with dilute HCl, water and dried. Concentration of the ether solution and trituration with ether-hexane gave a solid which on recrystallisation (ether-hexane) furnished the optically active vinyl carbinol 9 as a colourless crystalline solid, m.p. 89-91°C. Yield - 1.87 g (85%). $[\alpha]_D^{25}$ + 178° (C = 0.017, $CHCl_3$), UV λ_{max}^{MeOH} 253 nm (ϵ = 13,564), IR (KBr) λ max (cm^{-1}), 3600 (-OH), 1650 (conjugated C=O), 1610 (C=C). PMR ($CDCl_3$/TMS) values : 1.3 (s, 3H, ang.CH_3), 1.8 (s, 3H, vinyl CH_3), 1.9-2.8 (m, 11H, methylenes and -OH), 5 - 6.3 (m, 3H, -CH=CH_2), CD (C = 0.495, Dioxan) λ nm: 320, 243, 213, Δ E : -0.78, + 7.62, + 6.05. These C.D. data are similar to those of the carbinol 15 given below: λ nm : 320-330, 237, 208 $[\theta]$obs : -0.0051, + 0.022, + 0.038. Analysis $C_{14}H_{20}O_2$ requires C = 76.33, H = 9.15%, Found C = 76.21, H = 9.11%.

Rearrangement of optically active ethynyl carbinol 8

i) With potassium hydride in tetrahydrofuran

To a suspension of KH (0.6 g of 35% dispersion in mineral oil) washed with 10 ml portions of dry petroleum ether in dry THF (20 ml) was added the ethynyl carbinol 1R, 8aS(+) 8 (1.1 g, 0.005 mole) in dry THF (20 ml) at 0-5° with constant stirring under nitrogen atmosphere. The reaction mixture was stirred for 3 hr at 0-5° and for 1 hr at room temperature and then quenched by the addition of saturated ammonium chloride solution. THF was removed by distillation under reduced pressure. The residue was taken up in chloroform and the chloroform solution was successively washed with brine, water and dried. Concentration of the dried extract furnished a viscous liquid which was chromatographed over silica gel.

Elution with 20% ethyl acetate-hexane gave the optically active ring enlarged dione 10 as a colourless solid; m.p. 61-63°C $[\alpha]_D^{25}$ + 293° (C = 0.017, $CHCl_3$). After three recrystallisations (chloroform-hexane) the pure material melted at 64.5-65.5°C. Yield - 0.41 g (40%). $[\alpha]_D^{25}$ + 335° (C = 0.05, $CHCl_3$). UV λ_{max}^{MeOH} 218 nm (E, 2893), IR(KBr) λ max 1720 cm^{-1} (C=O), 1680 cm^{-1} (conjugated C=O), 1620 cm^{-1} (C=C), PMR (CCl_4/TMS) δ values : 1.3 (s, 3H, ang. CH_3), 1.65 (s, 3H, vinyl CH_3), 1.8-2.7 (m, 10H, methylenes), 5.5 (s, 2H vinyl protons), CD(C = 0.487, Dioxan) λ nm 300-305, 225-230, 210, Δ E +4.41, -3.58, +1.91. Mass spectrum : m/e 218; Analysis $C_{14}H_{18}O_2$ requires C = 77.06, H = 8.2%, Found : C = 77.31, H = 8.1%. Further elution with 30% ethyl acetate-hexane gave the starting optically active ethynyl carbinol (0.51 g, 46%) with the same specific rotation.

ii) With catalytic amount of sodium methoxide in methanol

To a solution of sodium methoxide (prepared from 0.02 g of sodium) in dry methanol (25 ml) was added ethynyl carbinol 1R, 8 aS (+)8 (1.1 g, 0.005 mole and mixture stirred at room temperature for 15 hr. Methanol was removed by distillation under reduced pressure. The residue was taken up in chloroform and the chloroform solution was washed with brine, water and dried. Removal of the solvent by distillation afforded a viscous liquid which was chromatographed over silica gel. Elution with 20% ethyl acetate-hexane gave a viscous liquid. $[\alpha]_D^{25}$ 0°. Yield = 0.22 g (20%). TLC, IR and PMR were comparable to those of the optically active compound obtained by the rearrangement of the ethynyl carbinol with KH in THF.

Further elution with 30% ethyl acetate-hexane gave the recovered optically active ethnynyl carbinol 8 (0.41 g, 40%) having same specific rotation.

iii) With catalytic amount of potassium methoxide in dry tetrahydrofuran

To a stirred suspension of potassium methoxide (prepared by dissolving 0.01 g of potassium metal in dry methanol and drying at 80°C under 20 mm vacuum for 1 hr) in dry THF (20 ml) was added the optically active ethynyl carbinol 8 (0.5 g, 0.0026 mole) in dry THF (10 ml) at 0-5°C under nitrogen atmosphere and mixture stirred for 3 hr. The reaction mixture was quenched by the addition of saturated solution of ammonium chloride. THF was removed by distillation under reduced pressure and the residue was taken up in chloroform. The chloroform solution was washed with brine, water and dried. Concentration of the dried extract furnished a viscous liquid which was chromatographed over silica gel. Elution with 20% ethyl acetate-hexane gave the optically active ring enlarged dione 10 as a crystalline solid; m.p. 63-65°C, Yield-0.15 g (30%). $[\alpha]_D^{25}$ + 318° (C = 0.041, $CHCl_3$). Further elution with 30% ethyl acetate-hexane yielded the starting optically active ethynyl carbinol 8 (0.15 g, 30%) having same specific rotation.

Reaction of optically active dione 10 with an equivalent amount of KOMe/MeOH

A suspension of potassium methoxide (prepared from 0.07 g of potassium metal dissolved in dry methanol and dried at 80°C/20 mm for 1 hr) in dry THF (20 ml) was stirred with the optically active dione 10 (0.5 g, 0.0018 mole) in dry THF (10 ml) at 0-5° under nitrogen atmosphere for 1 hr and then at room temperature for 1 hr. The reaction mixture was quenched by the addition of a saturated solution of ammonium chloride. THF was removed by distillation under reduced pressure and the residue was taken up in chloroform. The chloroform solution was washed with brine followed by water and dried. Concentration of the dried extract gave a viscous liquid. Yield = 0.3 g (75%) $[\alpha]_D^{25}$ + 215° (C = 0.05, $CHCl_3$). TLC of this liquid showed it to be a mixture of two compounds after multiple elution. The spectral data (IR, PMR) were found to be identical with those of the mixture obtained by the treatment of the ethynyl carbinol 8 with an equivalent amount of potassium methoxide in dry THF. The viscous liquid was chromatographed over neutral alumina. Careful elution with 5% ethyl acetate - hexane afforded the optically active starting dione 10 as colourless solid, m.p. 62-64°C. Yield = 0.08 g (20%) $[\alpha]_D^{25}$ + 320° (C = 0.05, $CHCl_3$). Further elution with 15% ethyl acetate - hexane gave a product which was found to be a multispotted material (TLC).

Effect of sodium methoxide on the optically active dione 10 in methanol

A solution of sodium methoxide (from 0.02 g of sodium) dissolved in dry methanol (10 ml) was stirred with the optically active dione 10 (0.22 g, 0.001 mole) in dry methanol (5 ml) at room temperature for 15 hr. Methanol was removed by distillation under reduced pressure and the residue was taken up in chloroform. The chloroform solution was washed with brine, water and dried. Removal of the solvent by distillation afforded a viscous liquid which was purified by passing through a column of silica gel (20% ethyl acetate - hexane) to give the starting optically active dione 10 (0.18 g, 90%) $[\alpha]_D^{25}$ + 330° (C = 0.05 g, $CHCl_3$).

Rearrangement of the optically active vinyl carbinol 9

i) With potassium hydride in tetrahydrofuran

A suspension of KH (0.6 g of 35% dispersion in mineral oil) washed with 10 ml portions of dry petroleum ether in dry THF (25 ml) was stirred with the vinyl carbinol 1R, 8 aS(+) 9 (1.1 g, 0.005 mole) at 0-5°C, under nitrogen atmosphere for 4 hr and then at room temperature for 1 hr. The reaction mixture was quenched by the addition of saturated solution of ammonium chloride and worked up as described in the case of the ethynyl carbinol (+)8 to furnish a viscous liquid which was chromatographed over neutral alumina. Elution with 20% ethyl acetate-hexane afforded a viscous liquid 11 which solidified when left in the refrigerator overnight. m.p.53-56°C. Yield = 0.3 g (30%) $[\alpha]_D^{25}$ + 18.2° (C = 0.017, $CHCl_3$). The recrystallized material melted at 55-57°C with $[\alpha]_D^{25}$ + 20.2°(0.023, $CHCl_3$). UV : λ_{max}^{MeOH} 224 (ε, 760); IR ($CHCl_3$) ν_{max} 1700 cm^{-1} (>C = O). PMR(CCl_4/TMS) δ values : 1.05 (s, 3H, ang.CH_3), 1.65 (s, 3H, vinyl CH_3), 1.75-2.8 (m, 14H, methylene protons). CD(Dioxan) nm 315-327, 233 $[\theta]$obs +0.0016, +0.0042. Mass spectrum : m/e 220. Analysis : $C_{14}H_{20}O_2$ requires C, 76.33, H,9.15; Found C, 76.31, H, 9.23%. Further elution with 30% ethyl acetate-hexane furnished a colourless liquid 17. Yield = 0.3 g (30%). $[\alpha]_D^{25}$ + 24° (0.017, $CHCl_3$). UV λ_{max}^{MeOH} 254 nm (ε, 16,280), IR($CHCl_3$) ν_{max} 1700 cm^{-1} (>C=O), 1660 cm^{-1}(conjugated C=O), 1605^{-1} (>C=C<). PMR (CCl_4/TMS) δ values : 1.15 (s, 3H, ang. CH_3), 1.7 (s, 3H, vinyl CH_3), 1.9-2.8 (m, 14H, methylene protons). CD (Dioxan) nm λ 330,257 $[\theta]$obs -0.0091, + 0.0021. Mass spectrum m/e 220. Analysis $C_{14}H_{20}O_2$ requires C = 76.33, H = 9.15 Found : C = 76.21, H = 9.10%.

ii) With methanolic potassium hydroxide

A solution of the vinyl carbinol 1R 8 aS(+)9 (0.5 g, 0.0023 mole) in methanol (25 ml) and aqueous potassium hydroxide (5%, 10 ml) was refluxed on a water bath for 30 min. Methanol was completely removed under reduced pressure and the residue was worked up to give a viscous liquid. It was purified by passing through a column of neutral alumina (20% ethyl acetate-hexane) to give a viscous liquid (11). Yield 0.25 g (50%)$[\alpha]_D^{25}$ 0°. IR and NMR were comparable with those of the optically active dione 11.

Catalytic hydrogenation of the optically active diketone 10

i) Using 10% Pd-C

A solution of the optically active dione 10 (0.3 g, 0.0014 mole) in dry ethyl acetate (10 ml) was hydrogenated in the presence of 10% Pd-C (0.05 g) at 50 psi for 3 hr. The catalyst was filtered and washed twice with 20 ml portions of dry ethyl acetate. Concentration of the filtrate gave a viscous liquid which was purified by passing through a column of neutral alumina (25% ethyl acetate - hexane) to furnish a colourless crystalline solid 18, m.p. 100-102°C. Yield = 0.21 g (70%). $[\alpha]_D^{25}$ + 258° (C = 0.023, $CHCl_3$). IR(KBr)ν_{max}: 1705 cm^{-1} (C=O), 1670 cm^{-1} (conjugated C=O), 1610 cm^{-1} (-C=C-). PMR($CDCl_3$/TMS) δ values 1.3 (merged doublet, 3H, $-CHCH_3$), 1.35 (s, 3H, ang.CH_3), 1.5-2.6 (m, 12H, methylenes and methine protons), 5.4 (d, 1H, vinyl H_α), 5.8 (d, 1H, vinyl H_β). Analysis : $C_{14}H_{20}O_2$ requires C = 76.33, H = 9.15%; Found C = 76.25, H = 9.21%

ii) Using PtO_2

A mixture of optically active dione 10 (0.3 g, 0.0014 mole) in dry methanol (10 ml) was hydrogenated in the presence of PtO_2 (0.05 g) at 50 psi. for 45 min. The catalyst was filtered, washed twice with 20 ml portions of dry methanol and the filtrate was concentrated to give a viscous liquid. This was chromatographed over neutral alumina. Elution with 20% ethyl acetate-hexane gave the optically active dione 11 as a low melting solid; m.p.53-56°C. Yield = 0.24 g (80%). $[\alpha]_D^{25}$ + 21° (C = 0.031, $CHCl_3$)

The spectral properties (IR, PMR) were identical with those of the optically active dione 11. Admixture with an authentic sample did not alter the m.p.

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