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Approaches to the synthesis of triterpenoids. IV. The ABC + E ring approach to the pentacyclic triterpene skeleton. Synthesis of a pentacyclic compound suitable for triterpene synthesis[1,2]

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Studies on the ABC + E ring construction of the pentacyclic triterpene skeleton are described. Acid-catalysed cyclisation of the mixture of diastereoisomers **11** led to preferential cyclisation of one isomer to 10-methoxy-2,2,4aβ,6aβ, 12bβ-pentamethyl-1,2,3,4,4a,5,6,6a, 6bα,7,8,12b,13,14-tetradecahydro-1-picenone (**12**). An X-ray analysis was performed on this compound which crystallizes in the monoclinic space group $P2/c$. There are four molecules in the unit cell which has dimensions $a = 6.456(2)$, $b = 42.518(6)$, $c = 8.519(2)$ Å, $\beta = 100.92(3)°$. The structure was solved by direct methods and refined by block-diagonal least-squares to a final R value of 0.042 for all 3234 observed reflections. The molecular structure found by X-ray diffraction confirms the stereochemical reasoning used in the synthetic steps.

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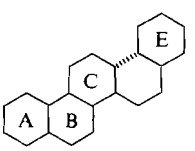
On décrit des études concernant la synthèse des cycles ABC + E du squelette pentacyclique des triterpènes. Une cyclisation acido-catalysée d'un mélange de diastéréoisomères de **11** conduit à la cyclisation préférentielle d'un isomère en méthoxy-10 pentaméthyl-2,2,4aβ,6aβ,12bβ tétradécahydro-1,2,3,4,4a,5,6,6a,6bα,7,8,12b,13,14 picénone-1 (**12**). On a effectué une analyse par rayon X de ce composé qui cristallise dans le groupe d'espace $P2/c$. Il existe quatre molécules par maille de dimension $a = 6.456(2)$, $b = 42.518(6)$, $c = 8.519(2)$ Å, $\beta = 100.92(3)°$. On a résolu la structure par des méthodes directes et on l'a affinée par la méthode des moindres carrés (blocs diagonaux) jusqu'à une valeur finale de R de 0.042 pour les 3234 réflexions observées. La structure moléculaire, qui a été déterminée par diffraction de rayon X, confirme le raisonnement stéréochimique utilisé dans les étapes de la synthèse.

[Traduit par le journal]

We wish to report recent studies aimed at a convergent synthesis[4] of the pentacyclic triterpene system (2) based on an ABC + E ring construction **1**, followed by formation of one bond (dotted in **1**) to



1

yield the polycyclic array. The advantage of this approach lies in the rapid provision of a polycyclic species with preformed stereochemistry, whereas the disadvantage lies in the control of stereochemistry during the vital cyclisation step.

Our basic strategy is outlined in Scheme 1. There exists a basic flaw in this plan in that the condensation of two racemates[5] **2** and **3** is unlikely to lead to any chiral induction in view of the distance between the reacting sites and any asymmetry and in fact it is reasonable to expect the production of a 50:50 mixture of the diastereoisomers **4***a*. However, at the outset we felt this route worth pursuing since we were of the opinion from inspection of molecular models and from the belief that the internal aldol-like process (**4***b* → **5**) necessitates a strict stereoelectronic arrangement for cyclisation (3, 4) that one of the diastereoisomers represented as **4***b* would cyclise preferentially *with respect to* the other, and it ap-

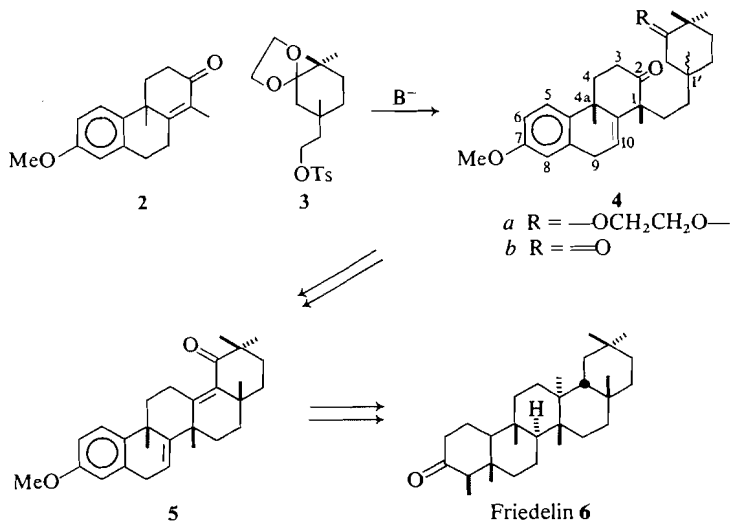
[1]Portions of this work are described in the Ph.D. thesis of S.B. (Carleton University, Ottawa, Ont. 1976). For Part III see ref. 1.

[2]NRCC No. 16712.

[3]To whom inquiries should be directed.

[4]For other successful triterpene syntheses see refs. 4–11 in Part III of this series (1).

[5]With the exception of structure **6**, which represents a natural product, all structures used in this paper represent racemates. Only that enantiomer bearing a direct relationship to the natural series is shown for convenience.

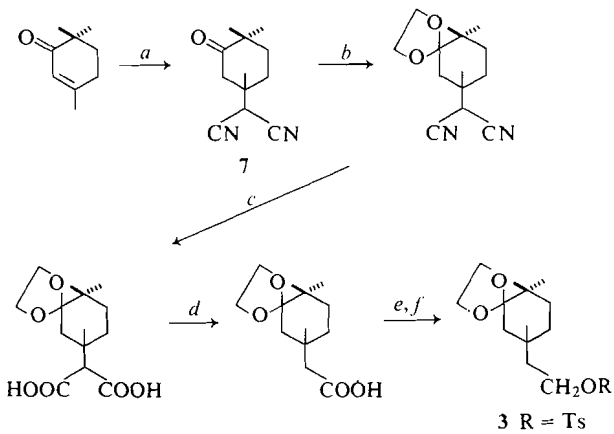


SCHEME 1

peared to us that the isomer cyclising should lead to **5** possessing the correct stereochemistry for further elaboration to friedelin **6**. Thus, although the basic strategy legislated for the loss of 50% of material, the other 50% should consist of a pentacyclic material close in structure to the target molecule. This surmise turned out to be at least partly correct as revealed in the sequel.

As starting material for our work we used tricyclic ketone **2** (5) and the tosylate **3**. The latter compound was available to us from the substituted malononitrile **7** obtained from the potassium fluoride catalysed Michael reaction between 3,3,6-trimethyl-2-cyclohexenone and malononitrile (6). A series of unexceptional steps as outlined in Scheme 2 led to the tosylate **3** in an overall yield of 26% from **7**.

Tricyclic enone **2** was alkylated via its dienolate ion



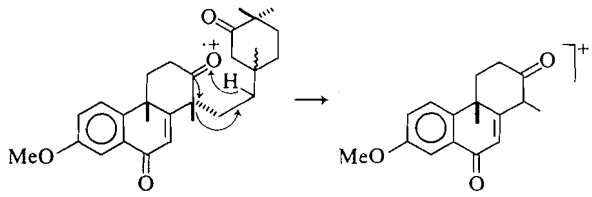
SCHEME 2. Reagents: (*a*) $CH_2(CN)_2$, KF; (*b*) $HOCH_2$-CH_2OH, *p*-TSA–H_2O; (*c*) KOH; (*d*) heat 140–145°C, 2 h; (*e*) $LiAlH_4$; *p*-toluenesulphonyl chloride, pyridine.

generated using potassium *tert*-amyloxide in dry benzene (7), with tosylate **3** to provide **4***a* in 54% yield, which crystallized although nuclear magnetic resonance spectroscopy and thin-layer chromatography indicated a mixture of diastereoisomers to be present. Acid hydrolysis of the ethylene ketal group provided the crystalline mixture of ketones **4***b*. The stereochemistry of the alkylation step at C(1) is based on the observations of previous workers (5,7,8) and on the use of benzene induced shifts of the methyl signals observed in the nmr spectra of our alkylated compounds (5). This assignment is confirmed by the X-ray structure determination quoted later.

Ketone mixture **4***b* was stable in crystalline form but solutions rapidly turned yellow with the formation of another species that was separated by column chromatography on alumina. This material is assigned structure **8** on the basis of its spectroscopic properties[6] including the appearance of the peak at *m/e* 270 in its mass spectrum, arising by cleavage as shown. Compound **8** could also be prepared from **4***b* on oxidation with Jones' reagent indicating the ease of oxidation of the C (9) benzylic-allylic position. Deoxygenated solutions of **4***b* were stable.

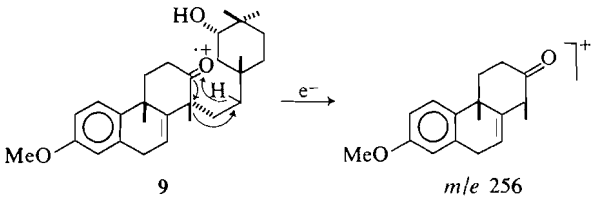
We next turned our attention to the cyclisation of the diketone mixture **4***b*. Attempts to effect the intramolecular aldol-like condensation using a variety of bases were singularly unsuccessful under a wide range of conditions. The use of *tert*-butylmagnesium chloride (9) as a cyclisation base at first seemed promising in that one component of the diastereoisomeric mixture reacted (tlc observation) while the other was inert under the conditions used. However, after isola-

[6]For brevity we chose to describe unexceptional spectroscopic values in the experimental section only.



8 *m/e* 270

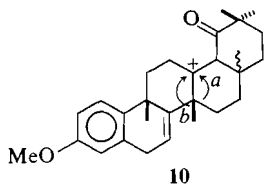
tion and characterisation it became apparent that simple carbonyl reduction had occurred by hydride transfer from the Grignard reagent (ref. 10 and refs. cited therein) to yield **9** in 39% yield from **4***b* (i.e.,



9 *m/e* 256

78% yield based on the reduction of one diastereoisomer). That the ring E carbonyl group had been reduced in this case was supported by the observation that the base peak in the mass spectrum of **9** appears at *m/e* 256 assigned as shown. Further comments on the stereochemistry depicted for **9** are presented later in this report.

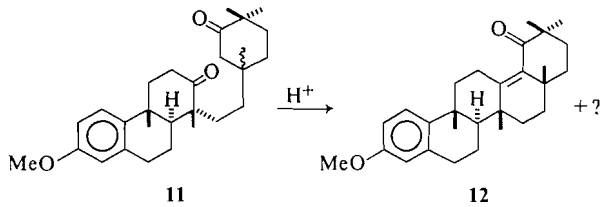
With the singular failure of base catalysis to induce cyclisation of **4***b* we next examined acid-induced reactions. In boiling xylene in the presence of *p*-toluenesulphonic acid, **4***b* yields a crystalline product mp 117–121°C whose physical properties indicated a structure far removed from the desired **5**. At first we suspected a simple rearrangement product arising from cation **10** via pathways *a* or *b*. However this



10

proved not to be the case. The structure of this product is discussed in the following paper (11).

It appeared to us that the failure of this cyclisation to provide pentacyclic species could lie in the lability of cation **10** leading to more stable allylic or benzylic species in competing processes. We therefore turned our attention to the cyclisation in the absence of the C(1a)—C(10) double bond in **4***b*. We have previously shown (5, 12) that hydrogenation of compounds related to **4** proceeds stereoselectively depending on the conditions used. In the event, reduction of mixture **4***b* by hydrogen in boiling xylene using palladium-on-charcoal as the catalyst was readily accomplished to yield the mixture of diketones **11**. Once again the stereochemistry assigned (5) to the new chiral centre at C-1a is based on the use of benzene-induced solvent shifts in the nmr spectrum of **11** (See Table 1).



11 **12**

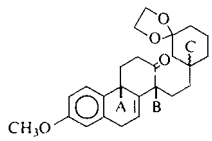
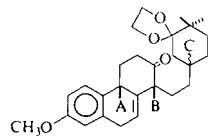
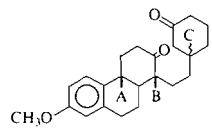
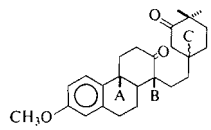
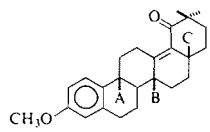
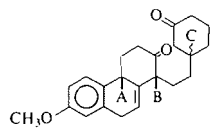
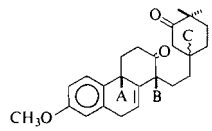
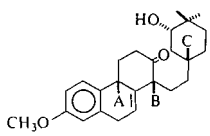
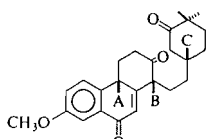
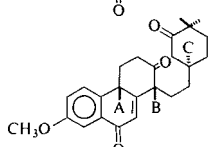
Reaction of **11** with *p*-toluene sulphonic acid in boiling xylene contradicted our prediction concerning the reactivity of one diastereoisomer compared to the other, since both components of the mixture **11** appeared to cyclise under these conditions. One reaction product crystallised after chromatography on silica gel. This material, mp 182–183°C was obtained in 90% yield based on the cyclisation of one diastereoisomer (i.e., overall 45% yield for this step). The other product from the cyclisation proved more difficult to purify and as yet has not been fully characterised. The crystalline product was assigned structure **12** based on its spectroscopic properties (see Experimental) and was simultaneously analyzed by X-ray diffraction.

Final parameters[7] from this analysis are listed in Tables 2 and 3, and a stereoscopic view of the molecular structure is shown in Fig. 1. This clearly confirms the above assignment, and underlines the sound basis for our other stereochemical predictions in this sequence. Figure 2 shows the final bond lengths, for which the estimated standard deviations are 0.002–0.003 Å. The bond lengths are very much as expected and require no special comments.

Endocyclic torsional angles are shown in Fig. 3. Ring A is approximately (within ±0.007 Å) planar, with distortions giving it a slight boat shape. Rings B and D have half-chair conformations, whereas rings C and E are chair shaped. The B/C ring junction is *trans*. There is some ring flattening in ring C near C(14) and in ring E near C(20). The three methyl groups at ring junctions are mutually *cis* and the ring system is convex toward them (cf. Fig. 1). The 1,3 diaxial methyl groups, C(24) and C(25), are separated by only 3.27 Å and this is despite an angle of 22.9° between the C(9)—C(24) and C(14)—C(25) vectors (which should in an ideal chair be parallel). The re-

[7]Tables of observed and calculated structure amplitudes and of bond angles are available, at a nominal charge, from the Depository of Unpublished Data, CISTI, National Research Council of Canada, Ottawa, Ont., Canada K1A 0S2.

TABLE 1. Benzene-induced solvent shifts and methyl group assignments in the nmr spectra of some synthetic compounds*

Compound	Methyl	$\delta CDCl_3$	δC_6D_6	Δ†
	A	80	88	−8
	B	70	65	+5
	C	52	54	−2
	A	81		
	B	70		
	C	51		
	A	71		
	B	62		
	C	50		
	A	75	65	+10
	B	67	62	+5
	C	52	45	+7
	A	79	73	+6
	B	67	60	+7
	C	59	55	+4
	A	80	82	−2
	B	71	64	+7
	C	50	38	+12
	A	80	84	−4
	B	71	63	+8
	C	48	37	+11
	A	80	86	−6
	B	70	65	+5
	C	58	58	0
	A	86	78	+8
	B	82	58	+24
	C	48	34	+14
	A	86	80	+6
	B	82	59	+23
	C	52	35	+17

*Determined at 60 MHz. Shifts are given in Hz downfield from internal TMS.
†$\Delta = \delta_{CDCl_3} - \delta_{C_6D_6}$.

pulsion between C(24) and C(25) is reflected also in lengthening of the C(9)—C(8) and C(8)—C(14) bonds (to 1.553 and 1.567 Å), and in opening of the C(9)—C(8)—C(14) angle (to 117.7°). C(25) and C(26), however, are 4.69 Å apart, and there is thus probably no repulsion between them. Despite the presence of the C(13)—C(18) double bond in the present compound, which partially flattens the ring C/D/E region, the general shape of this molecule is quite similar to that of epifriedelinol (13) and campanulin (14), another friedelin-type triterpene.

There is no apparent conjugation between the C(13)—C(18) double bond and the C(19)—O(2) carbonyl group; the C(13)—C(18)—C(19)—O(2) torsional angle is −66.7° and the C(18)—C(19) bond, 1.501 Å, is about 0.06 Å longer than expected for a conjugated system. The twist of C(19)—O(2) out of the C(12),C(13),C(18) plane is necessary to avoid too close a nonbonded contact with one of the hydrogen atoms on C(12).

Packing of the molecules in the crystal structure is governed by van der Waals forces; there are no hydrogen bonds or other short intermolecular contacts.

Thus, pentacyclic material **12** is easily obtainable in 16% yield from **2** and **3** and possesses four chiral centres corresponding to friedelin **6**. Work on its conversion to a triterpene as well as other applications of the described intramolecular cyclisation are in progress in our laboratory.

Earlier, structure **9** was assigned to the reduction product of mixture **4***b*, one of the diastereomeric constituents undergoing reduction whilst the other remained unchanged. This latter constituent was separated, hydrogenated and subjected to the acid-catalysed cyclisation process described above. No trace of pentacycle **12** could be detected from this reaction leading us to the conclusion that the C-1′ methyl group in this isomer is α oriented thus the reduction product is assigned a β-methyl group at the same position. The nmr spectrum of **9** exhibits a doublet of doublets at δ 3.40 that is partially hidden by the benzylic proton resonance, which being coupled to the olefinic proton, appears as a doublet. Decoupling of the olefinic proton causes the benzylic protons signal to collapse to a singlet and the doublet of doublets assigned to the carbinol hydrogen becomes clear. The coupling constants observed for this signal are 12 and 6 Hz, corresponding to an axial hydrogen in a cyclohexane flanked by one methylene group. This leads to the conclusion that the hydroxyl group is equatorial and that the complete stereochemical description of **9** is as shown. Attempts to oxidise **9** to the corresponding diketone for conversion to **12** were thwarted by the reactivity of the C-10 benzylic allylic position. Lack of material and other

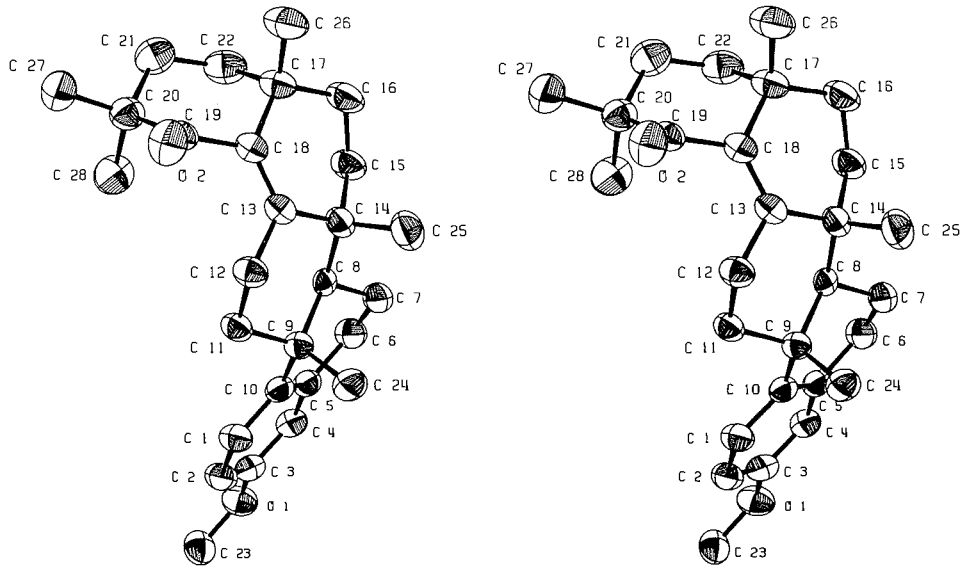


FIG. 1. A stereoscopic view of the compound **12** molecular structure, drawn with the ORTEP program (18). Thermal ellipsoids enclose 50% probability.

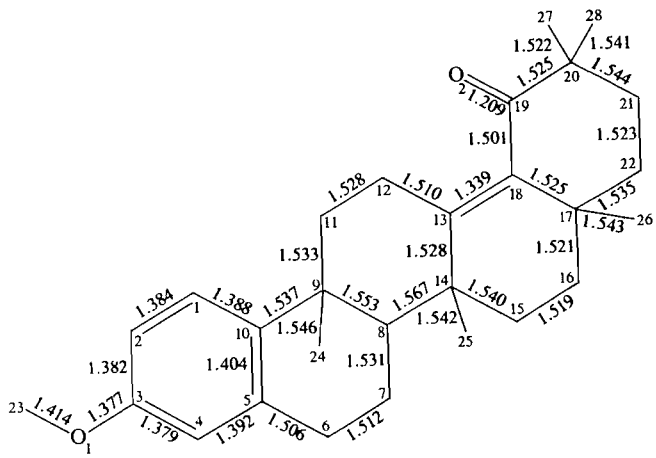


FIG. 2. Final bond lengths. The esd's are 0.002–0.003 Å.

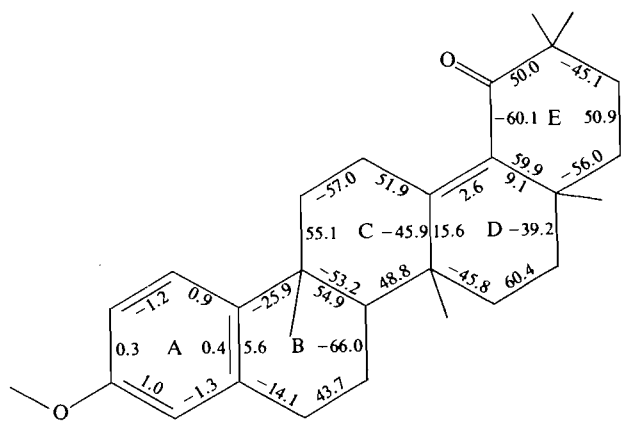
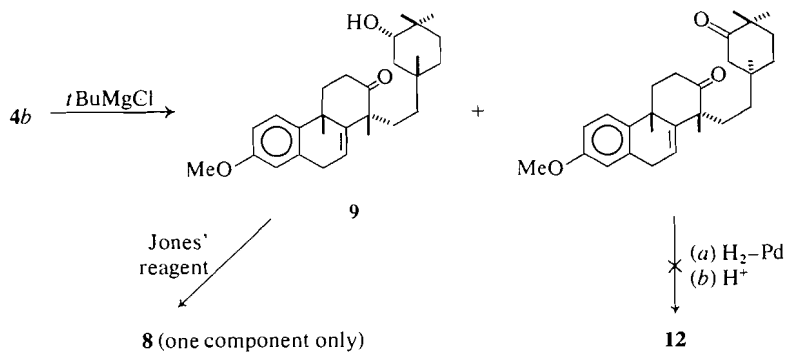
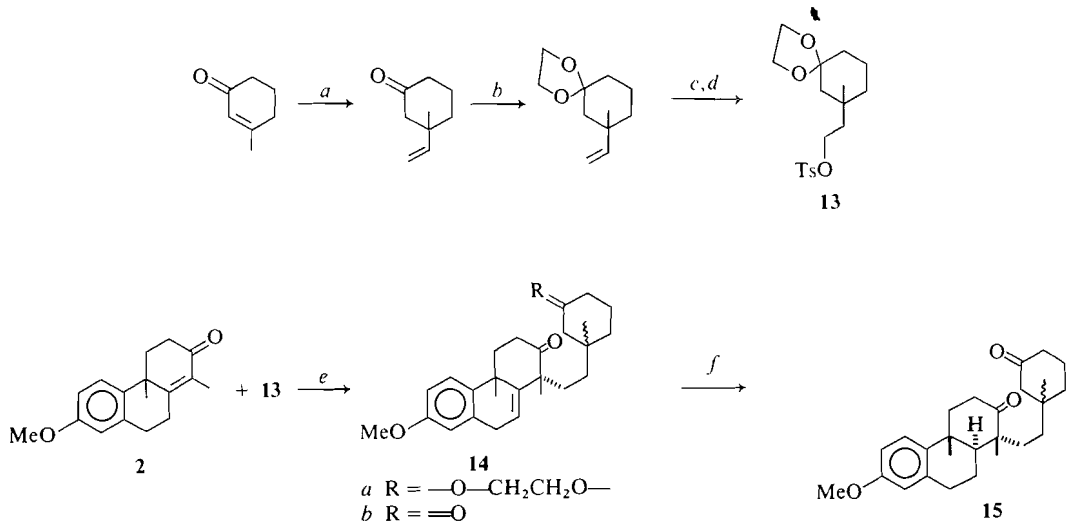


FIG. 3. Endocyclic torsional angles.



priorities have so far precluded further work on the finer details of this problem.

As already stressed we have often relied on benzene induced solvent shifts of the methyl group resonances in the nmr spectra of synthetic materials for the assignment of stereochemistry (cf. Table 1). In this particular study the spectra of compounds **4**, **8**, **9**, and **11** were complicated in the methyl region because of the presence of the *gem*-dimethyl system in the pendant potential E ring. In order to enable an unambiguous assignment of the methyl signals in the nmr spectra of our intermediate we undertook synthesis of tosylate **13** as outlined in Scheme 3; this, in turn was used to alkylate **2** to yield mixture **14***a* which was deketalised to **14***b* and hydrogenated to **15**. This route is reminiscent of that already described and served to confirm the assignment of nmr signals made previously. We did perform some cyclisation



SCHEME 3. Reagents: (*a*) CH_2=CHMgBr, CuI; (*b*) $HOCH_2CH_2OH$, H^+; (*c*) disiamylborane; (*d*) *p*-toluenesulphonyl chloride; (*e*) potassium *tert*-pentoxide; (*f*) Pd/C, H_2, xylene.

attempts on **14***b* and **15** but preliminary indications were not promising. We do not plan any further studies in this particular direction.

The original impetus for the work described herein came from the assumption that the optimum energy pathway for an internal aldol-like cyclisation is that by which the orbital overlap between the enolate π system of one ketone and that of the carbonyl group of the other occurs in a perpendicular manner (see **16**) modified by the suggestions of Burgi *et al.* (ref. 3, see also ref. 4) that nucleophilic attack on the carbon atom of a carbonyl group is directed down 'a funnel of reactivity' whose axis is slightly behind the perpendicular axis of the carbonyl group as in **17**. Inspection of molecular models can often distinguish between two possible modes of attack if severe steric interactions are to be avoided in any transition state assumed to take account of the restrictions summarised in **16** and **17**. In the cases we have reported this is obviously not the complete story but we have detected differences in reactivity toward cyclisation in work that is at present incomplete[8] that can apparently be explained using these concepts. The present

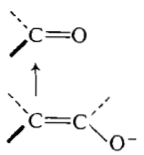
[8]D. T. Tho, A Greaves, and J. W. ApSimon. Unpublished observations.

TABLE 2. Final parameters (esd's) for the nonhydrogen atoms. The U_{ij} values are all $\times 10^{4}$*

Atom	x/a ($\times 10^4$)	y/b ($\times 10^5$)	z/c ($\times 10^4$)	U_{11}	U_{22}	U_{33}	$2U_{23}$	$2U_{13}$	$2U_{12}$
O(1)	5758(2)	−3392(3)	8164(1)	655(7)	440(9)	638(7)	−5(11)	430(12)	−161(11)
O(2)	10295(2)	18089(3)	3233(1)	549(7)	769(9)	467(6)	119(11)	363(10)	59(12)
C(1)	8729(3)	2415(4)	6283(2)	545(9)	375(9)	433(8)	−38(13)	286(14)	31(14)
C(2)	7579(3)	−271(4)	6446(2)	551(9)	385(9)	482(9)	−86(14)	216(14)	23(14)
C(3)	6901(2)	−797(3)	7868(2)	405(8)	366(9)	532(9)	95(13)	207(13)	86(12)
C(4)	7375(2)	1367(4)	9089(2)	471(8)	440(9)	464(9)	101(13)	283(13)	119(14)
C(5)	8497(2)	4101(3)	8915(2)	403(8)	394(9)	403(8)	41(13)	142(12)	153(12)
C(6)	8874(3)	6435(4)	10270(2)	642(10)	485(9)	381(8)	27(14)	274(15)	57(15)
C(7)	10487(3)	8936(4)	10110(2)	590(10)	449(9)	348(8)	−40(13)	70(13)	53(14)
C(8)	10129(2)	10177(3)	8394(2)	395(7)	385(9)	341(7)	−54(13)	76(12)	44(12)
C(9)	10575(2)	7519(3)	7251(2)	380(7)	357(9)	386(7)	−68(13)	152(12)	45(12)
C(10)	9206(2)	4658(3)	7480(2)	390(7)	357(9)	391(8)	22(13)	129(12)	176(12)
C(11)	9960(2)	8810(3)	5547(2)	465(8)	366(9)	356(7)	−133(13)	186(12)	−5(12)
C(12)	11076(2)	11894(3)	5309(2)	500(8)	394(9)	392(8)	−81(13)	312(13)	−4(14)
C(13)	10685(2)	14436(3)	6456(2)	376(7)	375(9)	392(7)	−117(13)	177(12)	−102(12)
C(14)	11131(2)	13485(4)	8218(2)	488(9)	403(9)	364(8)	−112(13)	78(13)	−70(14)
C(15)	10038(3)	15815(4)	9181(2)	808(12)	430(9)	369(8)	−153(14)	261(16)	3(16)
C(16)	10365(3)	19228(4)	8762(2)	850(13)	403(9)	475(10)	−258(14)	276(17)	−119(16)
C(17)	9504(3)	19982(3)	7014(2)	585(10)	348(9)	483(9)	−141(13)	326(15)	−34(14)
C(18)	9937(2)	17271(3)	5949(2)	405(8)	366(9)	412(8)	−92(13)	216(12)	−98(12)
C(19)	9165(2)	18006(3)	4214(2)	458(8)	330(9)	415(8)	−54(13)	203(12)	−122(12)
C(20)	6802(2)	18641(4)	3770(2)	434(8)	430(9)	566(10)	29(14)	153(14)	−45(14)
C(21)	6167(3)	21077(5)	4936(2)	559(10)	595(9)	718(12)	41(18)	317(18)	264(18)
C(22)	7106(3)	20484(4)	6690(2)	679(11)	513(9)	656(11)	−99(16)	584(18)	171(16)
C(23)	5318(3)	−5700(4)	6951(2)	670(11)	513(9)	580(11)	67(16)	42(17)	−292(18)
C(24)	12879(3)	6329(4)	7549(2)	428(8)	485(9)	591(10)	−49(14)	175(14)	149(14)
C(25)	13530(3)	13564(5)	8859(2)	556(10)	604(9)	568(11)	−59(16)	−103(16)	−274(16)
C(26)	10613(3)	22977(4)	6569(2)	838(13)	385(9)	633(11)	−123(16)	422(19)	−143(16)
C(27)	6202(3)	19845(5)	2061(2)	644(11)	614(9)	609(11)	132(18)	−103(17)	19(18)
C(28)	5674(3)	15484(5)	3902(3)	454(10)	614(9)	888(14)	218(20)	86(18)	−254(16)

*Thermal factor $\exp[-2\pi^2(U_{11}a^{*2}h^2 + \text{-------} + 2U_{23}b^*c^*kl + \text{-----} + \text{---})]$.

work falls nicely into the framework presented recently by Baldwin and co-workers (19) where orbital overlap considerations have been elegantly summarised in a series of rules for ring closure.



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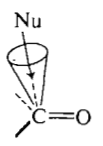

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Experimental

For general information concerning experimental procedures and spectroscopic analysis see Part III of this series (1).

*2-Keto-1β,4aβ-dimethyl-1α-[2-(1′,4′,4′-trimethyl-3′-ethylenedioxycyclohexyl)ethyl]-7-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene (**4**a)*

The method of Stork and Schulenberg (7) was followed. A mixture of potassium (810 mg, 20.78 mmol), *tert*-amyl alcohol (4 ml), and dry benzene (80 ml) was refluxed under a nitrogen atmosphere to give a solution of potassium *tert*-pentoxide. The tricyclic ketone **2** (5 g, 19.53 mmol) was added to the cooled solution and, while fresh benzene was being added, the reaction mixture was heated for 5 h to distill off a mixture of benzene – *tert*-pentyl alcohol. The resulting green-brown suspension of the potassium salt of **2** was cooled to room temperature and tosylate (solid) **3** (7.2 g, 18.8 mmol) was added. The mixture was refluxed for 2 h and then stirred at room temperature overnight. The greenish black syrupy mixture was poured into an ice–water mixture (250 ml) and acidified with 2 *N* H_2SO_4. The organic material was extracted with ether (×3) washed with ether (×3), washed with saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. Evaporation of the solvent gave a yellow oil which crystallized on standing. Recrystallization of this solid from methanol yielded light yellow crystals (4.58 g, 53.5%), mp 107–115°C. Two more recrystallizations furnished an analytical sample: mp 114–115°C; ir (Nujol): 1705 (C=O) and 1600 cm^{-1} (aromatic); nmr ($CDCl_3$) δ: 0.85 (s, 3, C-1 CH_3), 0.88 (s, 6, *gem*-dimethyl), 1.15 (s, 3, C-4a CH_3), 3.42 (d, 2, J = 4 Hz, C-9 CH_2), 3.78 (s, 3, —OCH_3), 3.83 (s, 4, —OCH_2—CH_2—O), 5.80 (t, 1, J = 4 Hz, C-10 H), and 6.67–7.33 (m, 3, ArH); ms *m/e* (relative intensity): 466 (14), 451 (7), 395 (21), 183 (100). *Anal.* calcd. for $C_{30}H_{42}O$: C 77.21, H 9.07; found: C 77.28, H 9.04.

*2-Keto-1β,4aβ-dimethyl-1α-[2-(3-keto-1,4,4-trimethylcyclohexyl)ethyl]-7-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene (**4**b)*

A solution of ketals **4***a* (4.58 g, 9.82 mmol) in methanol (100 ml) and 5% oxalic acid (enough to make the solution slightly turbid) was refluxed for 2 h. Water was added and the mixture extracted with ether (×3). The ether layer was washed with saturated solution of sodium bicarbonate, then water, and was dried over anhydrous sodium sulphate. Evaporation of the ether under reduced pressure gave a red oil. The oil was dissolved in 20 ml methanol and placed in the refrigerator overnight. The yellow crystals formed were isolated by filtration to give 2.7 g (65%) of the diketones **4***b*: mp 106–112°C; ir (Nujol): 1700 (C=O) and 1610 cm^{-1} (aromatic); nmr ($CDCl_3$) δ: 0.80 (s, 3, C-1′ CH_3), 0.98 (s, 3, C-4′ CH_3), 1.04 (s, 3, C-4′

TABLE 3. Final parameters (esd's) for the hydrogen atoms*

Atom	x/a ($\times 10^3$)	y/b ($\times 10^4$)	z/c ($\times 10^3$)	B (Å^2)
H(11)	921(2)	271(4)	527(2)	3.0(0.3)
H(21)	725(3)	−168(4)	557(2)	3.8(0.4)
H(41)	695(3)	94(4)	1013(2)	4.2(0.4)
H(61)	928(3)	537(4)	1127(2)	4.1(0.4)
H(62)	753(3)	745(4)	1029(2)	4.3(0.4)
H(71)	1193(3)	800(4)	1038(2)	4.1(0.4)
H(72)	1034(3)	1065(4)	1084(2)	4.3(0.4)
H(81)	852(2)	1051(4)	804(2)	2.6(0.3)
H(111)	841(2)	915(3)	528(2)	2.8(0.3)
H(112)	1027(3)	729(4)	476(2)	3.2(0.3)
H(121)	1069(3)	1255(4)	419(2)	3.5(0.3)
H(122)	1262(3)	1152(4)	545(2)	3.4(0.3)
H(151)	1060(3)	1549(4)	1035(2)	4.7(0.4)
H(152)	847(3)	1534(4)	900(2)	4.1(0.4)
H(161)	1189(3)	1972(5)	897(2)	4.5(0.4)
H(162)	962(3)	2051(5)	940(2)	4.8(0.4)
H(211)	456(4)	2121(5)	480(3)	6.1(0.5)
H(212)	659(3)	2320(5)	461(2)	5.4(0.5)
H(221)	647(3)	1861(5)	711(2)	5.1(0.4)
H(222)	681(3)	2226(5)	736(2)	4.8(0.4)
H(231)	447(4)	−724(5)	740(3)	5.9(0.5)
H(232)	671(3)	−668(5)	673(3)	5.5(0.5)
H(233)	458(4)	−492(5)	592(3)	5.9(0.5)
H(241)	1298(3)	438(5)	690(3)	5.5(0.5)
H(242)	1391(3)	781(5)	730(2)	4.9(0.4)
H(243)	1338(4)	564(5)	866(3)	5.8(0.5)
H(251)	1382(4)	1256(6)	986(3)	7.1(0.6)
H(252)	1442(4)	1248(6)	813(3)	6.5(0.5)
H(253)	1402(3)	1562(4)	895(2)	4.6(0.4)
H(261)	1017(4)	2358(5)	542(3)	5.9(0.5)
H(262)	1218(4)	2260(5)	683(3)	5.9(0.5)
H(263)	1029(3)	2477(5)	725(2)	5.4(0.4)
H(271)	665(4)	1826(6)	131(3)	6.6(0.5)
H(272)	470(4)	2037(7)	185(3)	8.0(0.6)
H(273)	699(4)	2174(6)	189(3)	6.5(0.5)
H(281)	628(4)	1385(6)	322(3)	6.8(0.6)
H(282)	416(4)	1575(5)	360(3)	6.0(0.5)
H(283)	603(4)	1467(5)	503(3)	5.9(0.5)

*Thermal factor exp $[-2\pi^2(U_{11}a^{*2}h^2 + \text{-------} + 2U_{23}b^*c^*kl + \text{-----} + \text{---})]$.

CH_3), 1.18 (s, 3, C-1 CH_3), 1.32 (s, 3, C-4a CH_3), 3.45 (d, 2, J = 4 Hz, C-9 CH_2), 3.84 (s, 3, OCH_3), 5.86 (t, 1, J = 4 Hz, C-10 H), and 6.60–7.40 (m, 3, ArH); nmr (C_6D_6) δ: 0.62 (s, 3, C-1′ CH_3), 0.88 (s, 3, C-4′ CH_3), 0.94 (s, 3, C-4′ CH_3), 1.06 (s, 3, C-1 CH_3), 1.41 (s, 3, C-4a CH_3), 3.24 (d, 2, J = 4 Hz, C-9 CH_2), 3.41 (s, 3, OCH_3), 5.68 (t, 1, J = 4 Hz, C-10 H), and 6.60–7.20 (m, 3, ArH); ms *m/e* (relative intensity): 422 (10), 389 (45), 256 (100). *Anal.* calcd. for $C_{28}H_{38}O_3$: C 79.57, H 9.06; found: C 79.37, H 9.07.

Jones' Oxidation of the Diones 4b

The pair of diastereoisomers, 4*b*, (50 mg) was dissolved in acetone (5 ml) and cooled in an ice-bath. Jones' reagent was added dropwise until an orange colour persisted. There was a green precipitate of chromous salt formed. After stirring for 1 h, water was added and the organic material extracted with ether (× 3). The ether layer was washed with water, saturated brine and dried ($MgSO_4$). Evaporation of the solvent gave 45 mg (90%) of the triones **8**. Two recrystallizations from methanol gave an analytical sample: mp 160–170°C; uv max (95% C_2H_5OH): 362 (10 900), 332 (2300), 224 (18 500), 212 nm (8200); ir (CH_2Cl_2): 1700 (C=O), and 1650 (C=O), 1605 cm^{-1} (aromatic, olefinic); nmr ($CDCl_3$) δ: 0.83 (s, 3, C-1′ CH_3), 1.03 (s, 6, *gem*-dimethyl), 1.37 (s, 3, C-1 CH_3), 1.43 (s, 3, C-4a CH_3), 3.90 (s, 3, O—CH_3), 6.50 (s, 1, C-10 H), 7.00–7.70 (m, 3, ArH); nmr (C_6D_6) δ: 0.62 (s, 3, C-1′ CH_3), 0.88, 0.97 (2 s, 3 each, C-4′ *gem*-dimethyl), 1.00 (s, 6, C-1 and C-4′ CH_3), 1.40 (s, 3, C-4a CH_3), 3.42 (s, 3, OCH_3), 6.55 (s, 1, C-10 H), and 6.71–8.00 (m, 3, ArH); ms *m/e* (relative intensity): 436 (100), 380 (80), 270 (65), 255 (70). *Anal.* calcd. for $C_{28}H_{36}O_3$: C 77.03, H 8.31; found: C 77.04, H 8.28.

The isomer *4b (C-1′ methyl α)* was similarly treated with Jones' reagent as above to give the trione ***8** (C-1′ methyl α)* in 93% yield: mp 183–185°C; ir (CH_2Cl_2): 1700 (C=O), 1650 (C=O), and 1605 cm^{-1} (aromatic, olefin); nmr (C_6D_6) δ: 0.58 (s, 3, C-1′ CH_3), 0.97, 0.98 (2 s, 3 each, C-4′ *gem*-dimethyl), 0.97 (s, 3, C-1 CH_3), 1.33 (s, 3, C-4a CH_3), 3.47 (s, 3, O—CH_3), 6.63 (s, 1, C-10 H), and 6.66–8.00 (m, 3, ArH); nmr ($CDCl_3$) δ: 0.86 (s, 3, C-1′ CH_3), 1.06 (s, 6, *gem*-dimethyl), 1.36 (s, 3, C-1 CH_3), 1.43 (s, 3, C-4a CH_3), 3.90 (s, 3, O—CH_3), 6.47 (s, 1, C-10 H), and 7.00–7.67 (m, 3, ArH); ms *m/e* (relative intensity) 436 (100), 380 (80), 270 (65), 255 (70). *Anal.* calcd. for $C_{28}H_{36}O_3$: C 77.03, H 8.31; found: C 77.15, H 8.29.

Attempted Cyclizations of Diones 4b

A solution of 1.06 g (2.51 mmol) diones *4b* in 60 ml dimethoxyethane (DME) under an argon sweep, was cooled in a Dry Ice – acetone bath and 14.5 ml of 1.1 *M* (15.95 mmol) *tert*-butylmagnesium chloride in THF was added through a septum by the aid of a syringe. The mixture was stirred for 1 h during which time a white precipitate was formed. This was then refluxed for 1 h and the solution became clear. The mixture was cooled and poured into a beaker containing ice and ammonium chloride (solid). This was extracted with ether (× 3) and the ether layer was washed with water, saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. Evaporation of the solvent gave an oil which, as shown by analytical thin-layer chromatography, contained two products. The mixture was separated by column chromatography using grade III aluminum oxide. Elution with petroleum ether gave compound *4b (C-1′ methyl α)* which corresponded to one of the starting diastereoisomers (75% recovery after recrystallization) and elution with 50% petroleum ether in benzene gave the new compound which was found to be the reduced product **9**, mp 133–135°C, 78.8% yield (based on one diastereoisomer). Two further recrystallizations afforded an analytical sample: ir (Nujol): 3450 (OH), 1700 (C=O), and 1605 cm^{-1} (aromatic, olefin); nmr ($CDCl_3$) δ: 0.78, 0.81 (2 s, 3 each, *gem*-dimethyl), 0.97 (s, 3, C-1′ CH_3), 1.23 (s, 3, C-1 CH_3), 1.33 (s, 3, C-4a CH_3), 3.43 (d, 2, J = 4 Hz, C-10 H), 3.40 (d of d, 1, J = 12 and 6 Hz, C-3′ H), 3.80 (s, 3, O—CH_3), 5.90 (t, 1, J = 4 Hz, C-9 H), and 6.67–7.43 (m, 3, ArH); nmr (C_6D_6) δ: 0.70, 0.75 (2 s, 3 each, *gem*-dimethyl), 0.97 (s, 3, C-1′ CH_3), 1.08 (s, 3, C-1 CH_3), 1.43 (s, 3, C-4a CH_3), 3.20 (d, 2, J = 4 Hz, C-9 H), 3.40 (s, 3, O—CH_3), 5.70 (t, 1, J = 4 Hz, C-10 H), and 6.53–7.33 (m, 3 ArH); ms *m/e* (relative intensity): 424 (10), 411 (14), 391 (50), 255 (100). *Anal.* calcd. for $C_{28}H_{40}O_3$: C 79.20, H 9.50; found: C 79.40, H 9.29.

Compound *4b (C-1′ methyl α)*: mp 118–122°C; ir: 1700 (C=O) and 1605 cm^{-1} (aromatic, olefin); nmr in $CDCl_3$ and C_6D_6 are identical to that of the mixture of diastereoisomers *4b*; ms *m/e* (relative intensity): 422 (10), 389 (45), 256 (100). *Anal.* calcd. for $C_{28}H_{38}O_3$: C 79.57, H 9.06; found: C 79.35, H 9.11.

Hydrogenation of 2-Keto-1,4a-dimethyl-1-[3-keto-1,4,4-trimethylcyclohexylethyl]-7-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene (4b)

A suspension of 500 mg of 10% palladium-on-charcoal in 15 ml *p*-xylene was hydrogenated at room temperature and atmospheric pressure for 4 h. Olefinic diketones *4b* (1 g) in

10 ml *p*-xylene were added and hydrogenated at atmospheric pressure at 140°C for 18 h. The solution was filtered and the *p*-xylene evaporated under reduced pressure. The resulting clear oil was dissolved in methanol and allowed to stand overnight during which time it crystallized to give 600 mg (60%) of the hydrogenated product **12**, mp 108–112°C. Two recrystallizations of a portion gave an analytical sample: mp 117–120°C; ir (Nujol): 1700 (C=O) and 1605 cm^{-1} (aromatic, olefin); nmr ($CDCl_3$) δ: 0.87 (s, 3, C-1′ CH_3), 1.08 (s, 3, C-4′ CH_3), 1.12 (s, 6, C-1, C-4′ CH_3), 1.26 (s, 8, C-4a CH_3), 3.78 (s, 3, —O—CH_3), 6.58 (d, 1, J = 3 Hz (*m*), ArC-8 H), 6.72 (d of d, 1, J = 9 (*o*) and 3 Hz (*m*), ArC-6 H), and 7.26 (d, 1, J = 9 Hz (*o*) ArC-5 H); nmr (C_6D_6) δ: 0.75 (s, 3, C-1′ CH_3), 0.86 (s, 3, C-4′ CH_3), 1.04 (s, 6, C-1, C-4′ CH_3), 1.09 (s, 3, C-4a CH_3), 3.42 (s, 3, O-CH_3), 6.56 (d, 1, J = 3 Hz (*m*) ArC-8 H), 6.74 (d of d, 1, J = 9 (*o*) and 3 Hz (*m*), ArC-6 H), and 6.96 (d, 1, J = 9 Hz (*o*) ArC-5 H); ms *m/e* (relative intensity): 424 (100), 409 (70), 391 (10), 367 (5), 258 (26), 243 (24). *Anal.* calcd. for $C_{28}H_{40}O_3$: C 79.20, H 9.50; found: C 79.24, H 9.59.

2-(3-Ethylenedioxy-1,4,4-trimethylcyclohexyl)malononitrile

Dicyanide **7** (6) (10 g, 0.049 mol) was dissolved in 400 ml benzene containing 15 ml ethylene glycol and 200 mg *p*-toluenesulfonic acid. This solution was refluxed for 24 h. The benzene layer was separated, washed with water, then with saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. After rotary evaporation of the solvent the product crystallized. Recrystallization from hexane yielded 11 g (90%) of the ketal: mp 91–93°C; ir (Nujol): 2250 cm^{-1} (C≡N), no carbonyl absorption; nmr ($CDCl_3$) δ: 0.90, 1.03 (2 s, 3 each, *gem*-dimethyl), 1.60 (s, 3, C-1 CH_3), 3.97 (s, 4, —O—CH_2—CH_2—O—), and 4.73 (s, 1, —$CH(CN)_2$). M^+ calcd. for $C_{14}H_{20}O_2N_2$: 248.1825; found: 248.1832.

2-(3-Ethylenedioxy-1,4,4-trimethylcyclohexyl)ethanoic Acid

A mixture of the above ketal dicyanide (14 g, 0.056 mol), ethylene glycol (32 ml) and potassium hydroxide (50 g, 0.893 mol) in 25 ml water was refluxed for 48 h. The reaction mixture was cooled to room temperature, acidified with cold 3 *N* H_2SO_4 (p*H* 4) and extracted twice with ether. The ether layer was washed with water, saturated sodium chloride, and dried over anhydrous magnesium sulphate. After evaporation of the solvent the crude diacid was decarboxylated by heating at 140–145°C (oil bath) during 2½ h. The nuclear magnetic resonance spectrum of this oil showed that the product had been deketalized. The oil was taken up in benzene; *p*-toluenesulfonic acid (200 mg) and ethylene glycol (15 ml) were added and the mixture refluxed overnight through a Dean–Stark trap. Separation of the benzene layer followed by washing with water, drying ($MgSO_4$), and rotary evaporation of the solvent gave 13.79 g (98%) of the monoacid as an oil. M^+ calcd. for $C_{13}H_{22}O_4$: 242.1518; found (mass spectrum): 242.1457.

2-(3-Ethylenedioxy-1,4,4-trimethylcyclohexyl)ethanol

To a suspension of 6.4 g (0.168 mol) of lithium aluminum hydride in dry diethyl ether (250 ml) was added dropwise 17.2 g (0.071 mol) of the above ketal acid. After completion of addition the mixture was refluxed overnight. The mixture was cooled to ice bath temperature and the excess lithium aluminum hydride was decomposed by careful addition of a saturated solution of Rochelle salt. The ether layer was separated and the aqueous layer extracted twice with ether. The combined ether layer was washed with water, saturated sodium chloride, and dried ($MgSO_4$). Evaporation of the solvent gave 11.8 g of the alcohol which was used in the next reaction without further purification: ir (neat): 3350 cm^{-1} (OH) and no carbonyl absorption; nmr ($CDCl_3$) δ: 0.93 (s, 6, *gem*-dimethyl), 0.98 (s, 3, C-1 CH_3), 3.70 (t, 2, J = 7 Hz, CH_2OH), and 3.92 (s, 4, —O—CH_2—CH_2—O—). M^+ calcd. for $C_{13}H_{24}O_3$: 228.1725; found (mass spectrum): 228.1784.

2-(3-Ethylenedioxy-1,4,4-trimethylcyclohexyl)ethanol Tosylate (3)

The above ketal alcohol (20 g, 0.088 mol) was dissolved in 200 ml dry pyridine and this was cooled in an ice bath. *p*-Toluenesulfonylchloride (purified by recrystallization) (25.5 g, 0.134 mol) was added to the mixture and stirred until dissolved. The reaction mixture was left in the refrigerator overnight. Water was added and the crystals formed (34 g) were collected by filtration. Recrystallization from ether gave 23 g (69%) of pure tosylate **3**: mp 100–104°C; ir (Nujol): 1590 cm^{-1} (aromatic), no carbonyl or hydroxyl absorption; nmr ($CDCl_3$) δ: 0.88 (s, 3, C-1 CH_3), 0.92 (s, 6, *gem*-dimethyl), 2.43 (s, 3, Ar CH_3), 3.83 (s, 4, —O—CH_2—CH_2—O—), 4.08 (t, 2, J = 7 Hz, CH_2—OTs), 7.30 (d, 2, J = 8 Hz, ArH), and 7.75 (d, 2, J = 8 Hz, ArH). *Anal.* calcd. for $C_{20}H_{30}O_5S$ (M^+ 382): C 62.87, H 7.85, O 58.39; found (M^+ 382): C 62.88, H 7.75, O 58.27.

Oxidation of 2-Keto-1β,4aβ-dimethyl-1-(3α-hydroxy-1,4,4-trimethylcyclohexylethyl)-7-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene (9)

Alcohol **9** (50 mg, 0.12 mmol) was dissolved in acetone (5 ml) and cooled in an ice bath. Jones' reagent was added dropwise until a yellow colour persisted. A green precipitate of the chromous salt was formed. After stirring for 1 h at room temperature, water was added and the organic layer extracted with ether (×3). The ether extract was washed with water, saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. Evaporation of the solvent under reduced pressure gave an oil which was crystallized from ether to give 45 mg (90%) of trione **8** (C-1′ methyl β), mp 152–154°C. Two recrystallizations furnished an analytical sample: mp 182–183°C; uv max: 362 (10 900), 332 (2300), 224 (18 500), and 212 nm (8200); ir (CH_2Cl_2): 1700 (C=O), 1650 (C=O), and 1605 cm^{-1} (aromatic, olefin); nmr ($CDCl_3$) δ: 0.80 (s, 3, C-1′ CH_3), 1.03 (s, 6, *gem*-dimethyl), 1.37 (s, 3, C-1 CH_3), 1.43 (s, 3, C-4a CH_3), 1.43 (s, 3, C-4a CH_3), 3.90 (s, 3, OCH_3), 6.47 (s, 1, C-10 H), and 7.33–7.67 (m, 3, ArH); nmr (C_6D_6) δ: 0.57 (s, 3, C-1′ CH_3), 0.86, 0.93 (2 s, 3 each, *gem*-dimethyl), 0.96 (s, 3, C-1 CH_3), 1.30 (s, 3, C-4a CH_3), 3.33 (s, 3, O—CH_3), and 6.66–8.00 (m, 3, ArH). *Anal.* calcd. for $C_{28}H_{36}O_3$ (M^+ 436): C 77.03, H 8.31; found (M^+ 436): C 77.08, H 8.25.

10-Methoxy-2,2,4aβ,6aβ,12bβ-pentamethyl-1,2,3,4,4a,5,6,6a,6bα,7,8,12b,13,14-tetradecahydro-1-picenone (12)

A solution of 200 mg of diketones **11** and 200 mg of *p*-toluenesulfonic acid in 20 ml *p*-xylene under an atmosphere of nitrogen was refluxed for 16 h. Water was added and the benzene layer separated. The aqueous layer was extracted (×2) with ether. The combined extracts were washed with water, saturated sodium chloride solution, and dried over magnesium sulphate (anhydrous). Evaporation of the solvent gave an oil which was chromatographed on silica gel using increasing concentrations of ether in benzene as eluent. The major fraction (100 mg) was crystallized from methanol to give the pentacyclic ketone **12**, mp 145–150°C (45 mg, 47%). Two recrystallizations of a portion gave an analytical sample: mp 156–158°C; ir (neat): 1684 (C=O) and 1625, 1605 cm^{-1} (aromatic, olefinic); nmr ($CDCl_3$) δ: 0.98 (s, 3, C-4a CH_3), 1.04 (s, 3, C-2 CH_3), 1.08 (s, 3, C-2 CH_3), 1.12 (s, 3, C-6a CH_3), 1.31 (s, 3, C-12b CH_3), 3.78 (s, 3, O—CH_3), 7.56 (d, 1, J = 3 Hz (*m*), ArC-9 H), 7.68 (d of d, 1, J = 9 (*o*) and 3 Hz (*m*), ArC-11 H), and 7.70 (d, 1, J = 9 Hz (*o*), ArC-12 H); nmr (C_6D_6) δ: 0.92 (s, 6, C-4a and C-12 CH_3), 1.00 (s, 3, C-6a CH_3), 1.21 (s, 5, C-12 and C-12b CH_3), 3.42 (s, 3, —OCH_3), 6.60 (d, 1, J = 3 Hz (*m*), ArC-9 H), 6.70 (d of d, 1, J = 9 (*o*) and 3 Hz (*m*), ArC-11 H), and 7.03 (d, 1, J = 9 Hz (*o*), ArC-12 H); ms *m/e* (relative intensity): 406 (42), 187 (100). *Anal.* calcd. for $C_{28}H_{38}O_2$: C 82.71, H 9.42; found: C 82.66, H 9.48.

*1,2,3,4,4a,9-Hexahydro-7-methoxy-1α-[2-(3-ethylenedioxy-1-methylcyclohexyl)ethyl]-1β-dimethyl-2(1H)-phenanthrone (**14**a)*

A mixture of potassium metal (810 mg, 20.78 mmol), *tert*-pentyl alcohol (4 ml), and dry benzene (80 ml) was refluxed (4 h) under a nitrogen atmosphere to give a solution of potassium *tert*-pentoxide. The tricyclic ketone **2** (5 g, 19.53 mmol) was added to the cooled solution and while fresh benzene was being added, the reaction mixture was heated for 5 h to distill off a mixture of benzene – *tert*-pentyl alcohol. The resulting green-brown suspension of the potassium salt of **2** was cooled to room temperature and the tosylate **13** (solid) (6.67 g, 18.84 mmol) was added. The mixture was refluxed for 2 h and then stirred at room temperature overnight. The greenish black syrupy mixture was poured into an ice–water mixture (250 ml) and acidified with 2 *N* H_2SO_4. The organic material was extracted with ether (×3), washed with saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. Evaporation of the solvent gave a yellow oil which solidified on standing. Recrystallization of this solid from methanol yielded light yellow crystals (4.5 g, 53%), mp 88–97°C. Two more recrystallizations provided an analytical sample of the diastereoisomers **14***a*: ir (Nujol): 1700 cm^{-1} (C=O); nmr ($CDCl_3$) δ: 0.86 (s, 3, C-1′ CH_3), 1.16 (s, 3, C-1 CH_3), 1.33 (s, 3, C-1 CH_3), 1.33 (s, 3, C-4a CH_3), 3.47 (d, 2, J = 4 Hz, C-9 H), 3.80 (s, 3, O—CH_3), 5.86 (d, 1, J = 4 Hz, C-10 H), and 6.78–7.43 (m, 3, ArH); nmr (C_6D_6) δ: 0.90 (s, 3, C-1′ CH_3), 1.08 (s, 3, C-1 CH_3), 1.47 (s, 3, C-4a CH_3), 3.23 (d, 2, J = 4 Hz, C-9 H), 3.43 (s, 3, O—CH_3), 3.50, 3.53 (2 s, 4, —OCH_2—CH_2—O—), 5.70 (t, I, J = 4 Hz, C-10 H), and 6.57–7.23 (m, 3, ArH); ms *m/e* (relative intensity): 438 (31), 423 (57), 361 (25), 255 (100). *Anal.* calcd. for $C_{28}H_{38}O_4$: C 76.68, H 8.73; found (M^+ 438): C 76.54, H 8.70.

*3,4,4a,9-Tetrahydro-7-methoxy-1α-[2-(3-keto-1-methylcyclohexyl)ethyl]-1β,4aβ-dimethyl-2(1H)-phenanthrone (**14**b)*

The keto ketals **14***a* (1 g) were dissolved in 25 ml methanol and were heated to near boiling point. A solution of oxalic acid (5%) was added until the mixture was slightly cloudy. This mixture was refluxed for 2.5 h and water was added and the methanol was evaporated under reduced pressure. The aqueous layer was extracted with ether (×3). The ether extract was washed with saturated sodium bicarbonate solution, water and saturated sodium chloride solution and dried over anhydrous magnesium sulphate. Evaporation of the solvent gave an oil (749 mg, 83%) which appeared homogeneous by thin-layer chromatography. Crystallization from methanol gave light yellow crystals, mp 105–109°C. Two recrystallizations from methanol afforded an analytical sample: mp 117–120°C; ir (Nujol): 1700 (C=O) and 1605 cm^{-1} (aromatic, olefinic); nmr ($CDCl_3$) δ: 0.83 (s, 3, C-1′ CH_3), 1.18 (s, 3, C-1 CH_3), 1.13 (s, 3, C-4a CH_3), 3.43 (d, 2, J = 4 Hz, C-9 H), 3.82 (s, 3, OCH_3), 5.88 (t, 1, J = 4 Hz, C-10 H), and 6.73–7.38 (m, 3, ArH); nmr (C_6D_6) δ: 0.63 (s, 3, C-1′ CH_3), 1.07 (s, 3, C-1 CH_3), 1.37 (s, 3, C-4a CH_3), 3.27 (d, 2, J = 4 Hz, C-9 H), 3.47 (s, 3, —O—CH_3), 5.72 (t, 1, J = 4 Hz, C-10 H), and 6.67–7.10 (m, 3, ArH); ms *m/e* (relative intensity): 394 (10), 379 (10), 361 (22), 255 (100). *Anal.* calcd. for $C_{26}H_{34}O_4$: C 79.15, H 8.69; found: C 79.17, H 8.55.

*3,4,4a,9,10aα-Hexahydro-7-methoxy-1α-[2-(3-keto-1-methylcyclohexyl)ethyl]-1β,4aβ-dimethyl-2(1H)-phenanthrone (**15**)*

A suspension of 200 mg of 10% palladium-on-charcoal in 10 ml *p*-xylene was hydrogenated for 2 h at room temperature and atmospheric pressure. The olefinic diketones **14***b* (300 mg) in 10 ml *p*-xylene were added to the suspension of catalyst and the mixture hydrogenated at 140°C and atmospheric pressure for 18 h. The reaction mixture was filtered and the *p*-xylene evaporated under reduced pressure to give an oil (180 mg) homogeneous by thin-layer chromatography. Attempts to induce crystallization failed: ir (neat): 1700 cm^{-1} (C=O); nmr ($CDCl_3$) δ: 0.83 (s, 3, C-1′ CH_3), 1.03 (s, 3, C-1 CH_3), 1.18 (s, 3, C-4a CH_3), 3.70 (s, 3, OCH_3), and 6.50–7.27 (m, 3, ArH); ms *m/e*: 396 (M^+).

3-Methyl-3-vinylcyclohexanone

Copper(I) iodide (3.81 g, 0.02 mol) was suspended in 75 ml of dry ether in a 250 ml three-necked, round-bottomed flask under argon. This suspension was stirred and cooled to −90°C in a Dry Ice – ether bath. Vinyl lithium (18 ml of 2.2 *M* solution, 0.04 mol) was added. The mixture became viscous and yellow. After stirring for 15 min at −90°C, 3-methyl-2-cyclohexenone (3.3 g, 0.03 mol) was added during 5 min. The mixture was stirred for another 5 min and was then quenched with excess methanol. The organic material was extracted three times, each with 50 ml ether, and the combined ether extract was washed successively with water, 5% ammonium hydroxide solution, water, saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. After filtering off the magnesium sulphate, the ether was evaporated under reduced pressure to give an oil. This crude oil was distilled to yield 3.5 g (88%) of the product: bp 40–46°C/0.8 Torr; ir (neat): 1710 (C=O) and 1640, 990 cm^{-1} (—CH=CH_2). M^+ calcd. for $C_9H_{14}O$: 138; found (mass spectrum): 138.

1-Ethylenedioxy-3-methyl-3-vinylcyclohexane

3-Methyl-3-vinylcyclohexanone (13.2 g) was dissolved in 150 ml benzene. Ethylene glycol (10 ml) (excess) and *p*-toluenesulfonic acid (300 mg) were added and the mixture refluxed for 18 h while stirring vigorously. A Dean–Stark trap was used to separate the water formed. After the mixture was cooled, water was added, and the benzene layer was separated. The water layer was extracted with ether (×2) and the benzene and ether extracts were pooled together and washed with water, saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. After removal of the magnesium sulphate by filtration the solvents were distilled at the rotary pump to give an oil. Distillation gave the product in 79% yield: bp 35°C/0.1 Torr; ir (neat): 1635 (C=C), 1065, 1090, 1150, 1180 cm^{-1} (ketal group); nmr ($CDCl_3$) δ: 1.10 (s, 3, CH_3), 3.90 (s, 4, —O—CH_2—CH_2—O—), 5.97 (d of d, 1, J = 18 and 10 Hz, —CH=CH_2), and 4.90 (m, 2, —CH=CH_2); ms *m/e*: 182 (M^+). *Anal.* calcd. for $C_{11}H_{18}O_2$: C 72.49, H 9.95, M^+ 182; found: C 72.56, H 10.06.

2-(3-Ethylenedioxy-1-methylcyclohexyl)ethanol

Disiamylborane was prepared by the method of Brown and co-workers (20). A mixture of sodium borohydride (2.13 g, 0.056 mol) and 2-methyl-2-butene (15.3 ml, 10.2 g, 0.145 mol) in freshly distilled tetrahydrofuran (75 ml) was cooled in an ice bath under a nitrogen atmosphere. Boron trifluoride etherate (9 ml, 10.1 g, 0.07 mol) was added dropwise over a period of 30 min and left stirring for 90 min at 0°C. To this mixture was added the 1-ethylenedioxy-3-methyl-3-vinylcyclohexane (1.47 g, 0.008 mol) very quickly and left to warm to room temperature. After 3 h the flask was cooled in an ice bath and 30.1 ml of 3 *N* NaOH was added followed by 20.0 ml 30% H_2O_2 (cautiously). The tetrahydrofuran was evaporated and the resulting mixture extracted with ether. The ether layer was washed with water, then with saturated sodium chloride solution, and dried over anhydrous magnesium sulphate. After removal of the magnesium sulphate by filtration, the solvent was evaporated under reduced pressure to give an oil which was distilled to yield 0.95 g (58%) of the alcohol: bp 80–85°C/0.01 Torr; ir (neat): 3420 cm^{-1} (OH); nmr ($CDCl_3$) δ: 0.95 (s, 3, CH_3), 3.90 (s, 4, —O—CH_2—CH_2—O—), and 3.67 (t, 2, J = 7 Hz, CH_2—OH); ms *m/e*: 200 (M^+). *Anal.* calcd. for $C_{11}H_{20}O_3$: C 65.97, H 10.07; found: C 65.99, H 10.17.

2-(3-Ethylenedioxy-1-methylcyclohexyl)ethanol Tosylate (13)

2-(3-Ethylenedioxy-1-methylcyclohexyl)ethanol (10 g, 0.05 mol) was dissolved in 100 ml dry, distilled pyridine and cooled in an ice bath. Solid *p*-toluenesulfonyl chloride (11.2 g, 0.059 mol) was added and the mixture left in the refrigerator overnight. Water was added to this mixture and the crystals formed were collected by filtration (79%). The crude crystals were recrystallized twice from ether to give an analytical sample: mp 66–68°C; ir (Nujol): no hydroxyl or carbonyl absorption, 1590, 1450 cm^{-1} (aromatic); nmr ($CDCl_3$) δ: 1.00 (s, 3, CH_3), 2.53 (s, 3, Ar CH_3), 3.92 (s, 4, —O—CH_2—CH_2—O—), 4.17 (t, 2, J = 7 Hz, CH_2—OTs), 7.43 (d, 2, J = 8 Hz, ArH), and 7.90 (d, 2, J = 8 Hz, ArH); ms *m/e*: 354 (M^+). *Anal.* calcd. for $C_{18}H_{26}O_5S$: C 60.99, H 7.39, S 9.05; M^+ 354; found: C 61.08, H 7.28, S 9.17.

X-ray Data Collection

Compound **12** crystallized from methanol as colourless laths elongated along a^*. The specimen used for data collection was cut to approximate dimensions 0.5 × 0.3 × 0.5 mm, and was mounted with b^* as rotation axis. Crystal data are as follows.

$C_{28}H_{38}O_2$ fw = 406.6
Monoclinic, a = 6.456(2), b = 42.518(6), c = 8.519(2) Å, β = 100.92(3)° (based on λ(CuKα$_1$) = 1.54051 and λ(CuKα$_2$) = 1.54433 Å), V = 2296.1 Å^3. Z = 4, ρ_c = 1.176 g cm^{-3}, space group $P2_1/c$, μ(CuKα) = 5.59 cm^{-1}.

Intensity data were measured with a Picker four-circle diffractometer in the θ/2θ scan mode using scan ranges of 2–3° and a (2θ) scan speed of 2°/min. All measurements were made at room temperature with Ni-filtered Cu radiation. The intensity of a check reflection, monitored at intervals of about 30 reflections, showed only small random fluctuations, and these measurements were used to place all the intensities on a single (arbitrary) scale. All 3908 accessible (2θ ≤ 130°) independent reflections in the *hkl* and $\bar{h}kl$ octants were measured, and of these, 3234 were considered as observed. The remainder, with net counts less than 12 or less than $\frac{1}{10}$ of the total background, were excluded from the least-squares refinement. Structure-factor amplitudes were obtained after applying Lorentz and polarization corrections, and an extinction correction was applied at a later stage. Absorption corrections were considered unnecessary (μ = 5.6 cm^{-1}).

Structure Determination and Refinement

The structure was determined by the symbolic addition procedure, and refinement was by block-diagonal least-squares minimizing $\Sigma w(|F_o| - |F_c|)^2$. The weighting scheme used in the final stages of refinement was of the form:

$$w = w_1 \times w_2$$

where

$$w_1 = 1 \Big/ \left[1 + \left(\frac{F_o - 11.0}{8.0}\right)^2\right]$$

$$1.7 < F_o < 194$$

and $w_2 = 4 \sin^2\theta$ if $\sin^2\theta < 0.25$, otherwise $w_2 = 1$. Hydrogen atoms were all located on a difference map and were subsequently refined isotropically while nonhydrogen atoms were refined anisotropically. Scattering factor values for oxygen and carbon atoms were taken from Hanson *et al.* (15) and for hydrogen from Stewart *et al.* (16). In the final least-squares cycle the mean (shift/estimated standard deviation) was 0.08 and the largest shift was 0.38 σ. The final R value for all 3234 observed reflections was 0.042. A final difference – Fourier map showed no significant features. Computer programs used in the analysis were those of Ahmed *et al.* (17) and Johnson (18).

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