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# NEW GENERAL SYNTHESIS OF MEDIUM RING-LACTONES VIA A REGIOSELECTIVE β-SCISSION OF ALKOXYL RADICALS GENERATED FROM CATACONDENSED LACTOLS[1,2]

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Abstract—— We describe a new general method for the synthesis of medium-sized lactones based on ring-enlargement via a regioselective β-scission of alkoxyl radicals generated by photolysis from the hypoiodites of several catacondensed lactols. The syntheses of 9-membered lactones from 6/5 fused lactols, 10-membered lactones including a naturally occurring lactone, phoracantholide I, from 6/6 or 7/5 fused lactols, and 11-membered lactones from 7/6 or 8/5 fused lactols are shown to be achieved by the present method. This new method may have a potential for application to the synthesis of either smaller or larger-sized lactones.

The chemistry of medium- and large-ring lactones has attracted considerable attention recently because many of the molecules belonging to these groups have revealed diverse and significant biological activities.[3] The methods used to synthesize these classes of lactone so far publised have been broadly classified into the three categories:[4] (a) cyclization of ω-hydroxyacids.[5] (b) cyclization of straight chain esters by carbon-carbon bond formation,[6] (c) ring enlargement and/or fragmentation.[7,8]

Most syntheses of the medium-ring lactones achieved by fragmentation have utilized the ionic cleavage of the bridged bond of bicyclic compounds, following the example of Borowitz's synthesis of the medium-sized lactones by means of the oxidative cleavage of the bridged bonds of bicyclic enol ethers.[8]

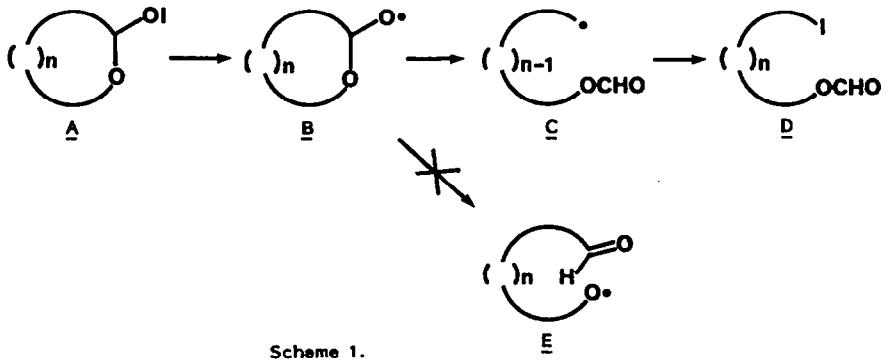
In this communication, however, we describe a new general method for the synthesis of medium-sized lactones based on a new ring-enlargement via a regioselective β-scission of alkoxyl radicals generated by the photolysis of catacondensed lactol hypoiodites.

In our previous papers,[9] we reported that the alkoxyl radicals B generated from lactol hypoiodites A undergo a regioselective β-cleavage of their C-C bond to give iodo formates D rather than a cleavage of their C-O bond to give species E (Scheme 1). We reasoned that the alkoxyl radicals of general type F, once generated from the photolysis of catacondensed lactol hypoiodites, may similarly undergo a β-scission of their C-C bonds and that the C-C bond which is cleaved preferentially may be the condensed bond a rather than b since the cleavage of the former gives a cyclic secondary carbon radical G while the latter gives a primary carbon centred radical I (Scheme 2). We found indeed that the β-scission of the alkoxyl radicals derived from the bicyclic lactols did take place in the direction we expected and we were thus able to achieve the synthesis of 9 to 11-membered lactones as described below. We also describe how application of this method enabled us to achieve a short-step synthesis of a naturally occurring 10-membered lactone, phoracantholide I [(±)-decan-9-olide].[10]

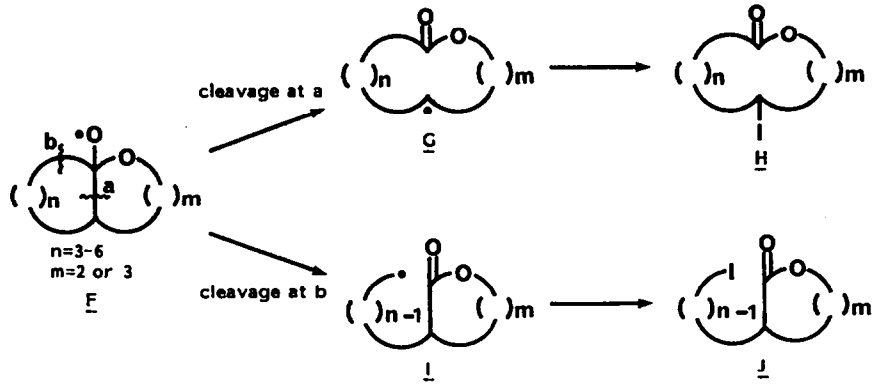
## Results

### Synthesis of 9-membered lactones (Scheme 3).

Synthesis of 9-membered lactones by the present method may be achieved through the β-scission of the alkoxyl radicals derived from either 5/6 (F, n=3, m=3) or 6/5




Scheme 1.



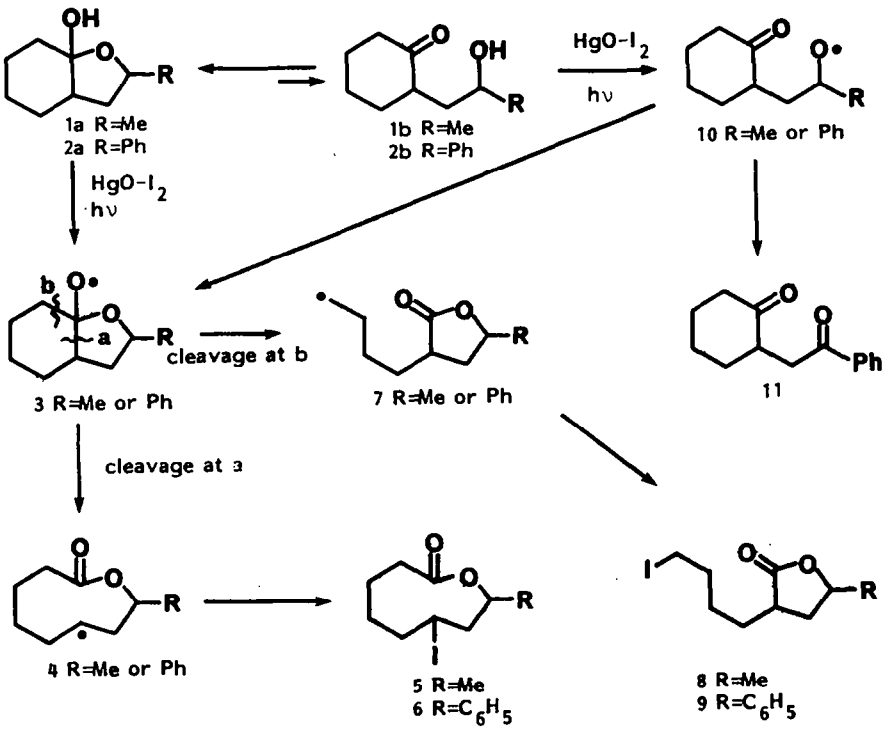

Scheme 2.

catacondensed lactols (F, n=4, m=2). We chose 2-(2-hydroxypropyl)-cyclohexanone (1b) and 2-(2-hydroxy-2-phenylethyl)cyclohexanone (2b) prepared by Britten and his colleagues[11] as the model substrates. The $^1$H NMR and IR spectra of these hydroxyketones (1b, 2b) indicated that these predominantly took the form of lactols (1a, 2a) in solution and showed that the ratios of the lactol 1a to the hydroxyketone 1b and 2a to 2b were approximately 2 to 1 and 2.2 to 1 by comparing the signal areas of the protons attached to their carbon atoms carrying etherea' oxygens of the lactols with those of the corresponding protons of the hydroxyketones. The catacondensed lactol 1a in benzene containing mercury(II) oxide and iodine (2 mol. equiv. each) together with a small amount of pyridine in a Pyrex vessel was irradiated with a 100-W high pressure mercury arc for 4 h to yield a mixture of products. The saparation of the products by preparative TLC gave a 3.5:1 mixture of the stereoisomers of ring-expanded 9-membered lactones 5 in a 53% yield and 8 in a 10% yield. The ratio of cis iodolactone 5 to trans isomer was deduced by $^1$H NMR, IR, and MS spectrometry: high-resolution mass spectrometry of the isomeric lactones 5 and 8 indicated the molecular formula $C_9H_{25}IO_2$ for both lactones, while IR spectrum of a 3.5:1 mixture of stereoisomeric lacones 5 exhibited a band due to the unstrained lactone carbonyl at 1728 cm$^{-1}$. The $^1$H NMR spectrum indicated an overlapping multiplet signal centred at $\delta$ 4.37, due to the methine protons carrying an iodine atom of cis and trans lactones, and two multiplets centred at $\delta$ 4.87 and 5.12 due to the protons attached to the carbons carrying the ethereal oxygens of the cis and trans isomers. The ratio of the signal at $\delta$ 4.87 to that at $\delta$ 5.12 was 3.5:1 but we were unable to determine which signal is due to cis or which to trans. The IR spectrum of isomeric lactone 8, on the other hand, exhibited a band at 1763 cm$^{-1}$ characteristic of the $\gamma$-lactone group while its $^1$H NMR spectrum showed a triplet signal at $\delta$ 3.20 assignable to the

methylene proton with an iodine atom and an overlapping multiplet ranging from δ 4.36 to δ 4.77 due to the protons attached to the carbons carrying the ethereal oxygens of the cis and trans isomers.

Irradiation of the catacondensed lactol 2a under similar conditions gave a 6:1 mixture of two stereoisomeric lactones 5 (52%) together with two stereoisomeric γ-lactones 9 (4% and 7%) and a diketone 11 (11%). The structure of diketone 11 was deduced by means of spectroscopy as well as from its synthesis by oxidation of lactol 2a with pyridinium chlorochromate (PCC) (Scheme 3). The pathways of the formation of all the products are outlined in Scheme 3. A portion of the 9-membered lactones 5 and 6 can be formed from the ring-opened alkoxyl radical 10 via the alkoxyl radical 3. This possibility will be discussed later in the paper. Diketone 11 is formed by the disproportionation of the alkoxyl radical 10. Our experiment confirmed that β-cleavage of alkoxyl radicals 3 takes place largely in the direction we expected, although unignorable amounts of a product arising from the primary radicals 7 are formed. No attempt has been made to calculate the difference in energy between the secondary radical 4 and the primary radical 7 since it is unlikely to be large enough for us to draw any conclusion as to whether the direction of the cleavage is partly controlled by a stereoelectronic factor.[12]

We then went on to the synthesis of 10-membered lactones.

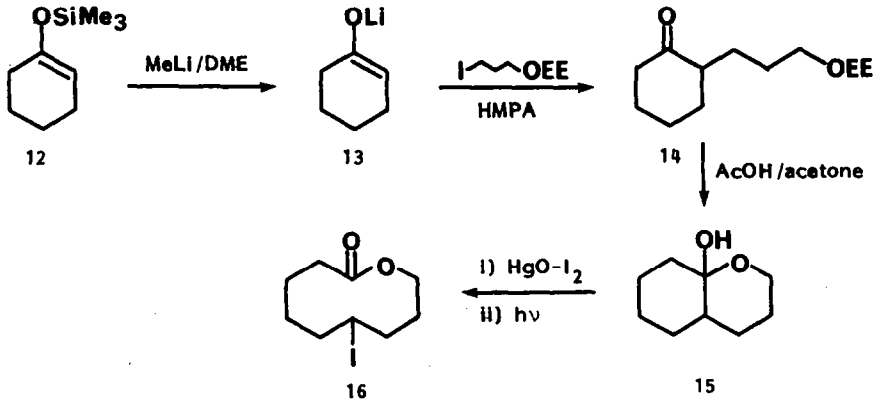



Scheme 3.

Synthesis of 10-membered lactones (Schemes 4, 5, 6, and 8).

Synthesis of 10-membered lactones by our method may be accomplished through the β-cleavage of the alkoxyl radicals generated from either 5/7 (F, n=3, m=5), 6/6 (F, n=4, m=4) or 7/5 (F, n=5, m=2) catacondensed lactols. We have in fact found that the 10-membered lactones can be obtained from both 6/6 and 7/5 fused lactols. We found, however, the 6/6 fused lactols are generally superior since they take the lactol forms in solution.

Trans-1-oxadecalin-9-ol (15) was chosen as the model of a 6/6 fused lactol. Alkylation of the lithium enolate 13[13] derived from silyl enol ether 12[14] with 1-iodo-3-(1-ethoxyethoxy)propane gave α-alkylcyclohexanone 14; this was then hydrolyzed with aqueous acetic acid-acetone[15] to give a trans-1-oxadecalin-9-ol (15).[8] In contrast to 6/5 fused lactols 1a and 2a, the $^1$H NMR and IR spectra of decalinol 15 indicated that it took the lactol form in solution. The lactol 15 was transformed into the corresponding hypoiodite with three equivalents each of mercury (II) oxide and iodine in benzene containing a small amount of pyridine. Irradiation of the solution with a 100-W high pressure Hg arc through a Pyrex filter gave 6-iodononan-9-olide (16), in a 79% yield. No δ-lactone corresponding to γ-lactone 8 or 9 arising from a primary carbon centred radical was formed in this reaction (Scheme 4). The high selectivity of this scission is remarkable.

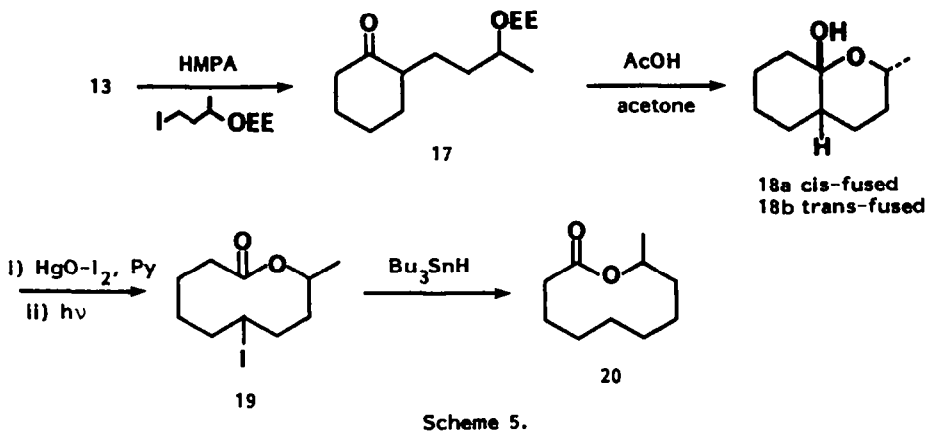



Scheme 4.

The utility of the present method can be demonstrated by the synthesis of (±)-Phoracantholide I. (R)-(-)-Phoracantholide I was isolated from the metasternal grand secretion of Phoracantha Synonima by Moore and Brown in 1976,[10] and since its isolation from the beetle, Phoracantholide I has been the target of several groups of synthetic organic chemists using a variety of approaches.[16,17]

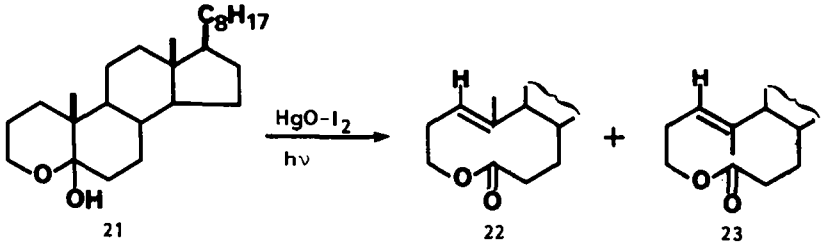
The lithium enolate 13 reacted with newly prepared 1-iodo-3-(1'-ethoxyethoxy) butane to give an α-alkylcyclohexanone 17. The removal of its protecting group by aqueous acetic acid-acetone at room temperature gave a 1:1 mixture of cis- and trans fused 1-oxa-2-methyldecalin-9-ols (18a and 18b);[16b] these were separable by means of TLC. The stereochemistry of the isomeric oxadecalinols was deduced by an $^1$H NMR spectra which showed that the chemical shifts of the methyls and the protons attached to their C-2 were nearly the same; this proved that the isomerism of the two products is not due to the relative configuration between their hydroxyl and methyl group. The treatment of the mixture of cis and trans isomers in benzene containing mercury (II) oxide, iodine and a few drops of pyridine, followed by irradiation under the same conditions as described for the synthesis of lactone 16 gave an iodophoracantholide I 19 in a 76% yield. The removal of its iodine with tributyltin hydride in benzene gave (±)-Phoracantholide I (20) in an 82% yield. Its various spectral data were in agreement with those published for this natural product. This synthetic sequence may perhaps be one of the simplest ever to have been reported for the synthesis of this natural lactone.

The synthesis of 10-membered lactones by the present ring enlargement method was then successfully applied to the synthesis of 10-membered steroidal lactones 22 and 23.[18] Thus, 4-oxa-5α- and 5β-cholestan-5-ols (21), after Edward et al.,[19] was subjected to β-scission under the conditions described above and gave two products 22 and 23 as outlined in Scheme 6. Spectral studies indicated that the major

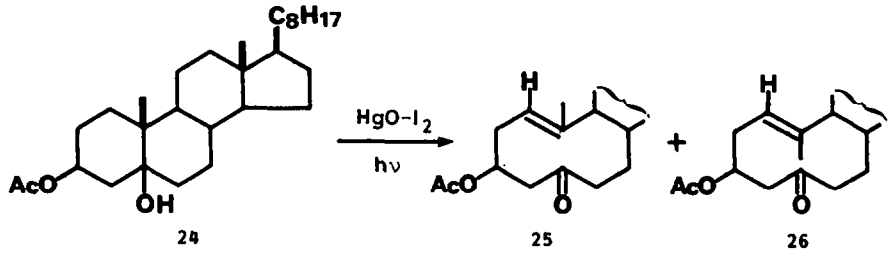



Scheme 5.

product (22) (28%) was its (Z)-isomer. The geometries of the double bonds of 22 and 23 were determined by their $^1$H NMR spectra. The $^1$H NMR spectrum of (Z)-isomer 22 exhibited an olefinic proton at δ 5.20 (ddd), while the olefinic proton of the (E)-isomer 23, due to a transannuler shielding by the 5-carbonyl group, appeared at a higher field (δ 5.07, ddd). The double bonds of lactones 22 and 23 are produced either by deprotonations of the intermediary carbocation generated by oxidation of carbon-centred radicals or by a two step process involving the initial formation of iodides followed by their dehydroiodination. This reaction is analogous to the hypoiodite reation of 1,8,8-trimethyl-3-oxabicyclo[3.2.1]oct-2-ol reported by us elswhere.[20] Mihailovic and his colleagues have reported[21] that irradiation of the hypoiodite of 5α-cholestan-3β,5β-diol 3-acetate (24) in the presence of mercury(II) oxide and iodine in benzene gave two products 25 and 26 arising from β-scission as outlined in Scheme 7. The difference in the chemical shifts of the olefinic protons of secosteroids 25 and 26 and those of oxasteroids 22 and 23 were found to be parallel.




Scheme 6.

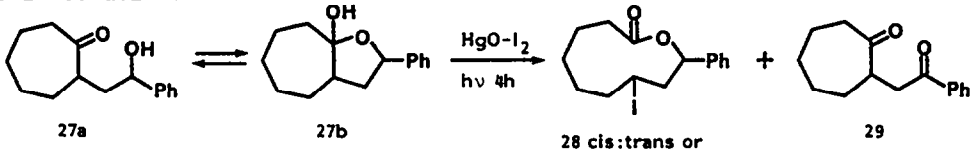



Scheme 7.

We were next able to confirm that 10-membered lactones can also be synthesized by the ring expansion of 7/5 fused lactols. We used a lactol 27b as a model which was derived from the 2-(2-hydroxy-2-phenylethyl)cycloheptanone (27a)[11]. The crystals of α-alkylcycloheptanone 27a prepared according to Britten's method were in the form of lactol 27b since its IR spectrum in Nujol showed no band due to a carbonyl

group. However, the IR and $^1$H NMR spectra of the solution ($CDCl_3$) indicated that it was in an equilibrium with a ring-opened form 27a. The $^1$H NMR spectrum of 27b in $CDCl_3$ (270 MHz) exhibited a quintet (J 4.4 Hz) centred at δ 4.69 due to the benzylic proton of the ring-opened form 27a, a doublet of a doublet centred at δ 5.02 (J 5.5 and 10.3 Hz) assignable to the benzylic proton of lactol form 27b and another doublet of a doublet centred at δ 5.15 (J 5.5 and 10.3 Hz) assignable to the isomeric lactol form 27b. The ratio of the area of the signal due to the benzylic proton of the ring-opened form 27a to those of the lactol form 27b was 1 to 4. Thus, equilibrium favours the lactol 27b susceptible of ring expansion and the lactol form 27b is a mixture of two isomers (most probably cis and trans form as depicted in Scheme 8). Irradiation of the hypoiodite resulted in the formation of a mixture of cis and trans 10-membered lactone 28 (81%) and α-(2-oxocycloheptyl)acetophenone (29) (9%). The ratio of the isomers in the iodolactone (28) was judged to be 1:1.8 by the $^1$H NMR spectrum.

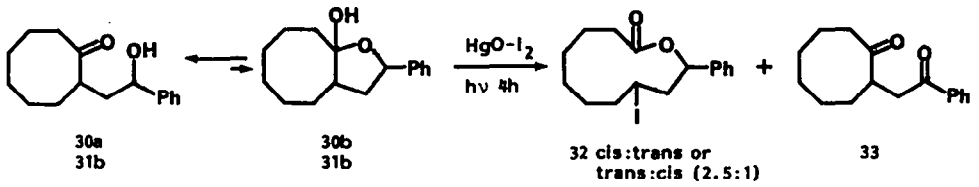
A high yield (81%) of lactone 28 is remarkable in view of the equilibrium between the open-chain form 27a and the lactol form 27b found in $CDCl_3$. The high yield of the lactone might be due to a different equilibrium in benzene which favours the formation of the lactone or may be due to a continuous shift of the equilibrium to lactol form 27b with the disappearance of the lactol. There is another possibility: part of the alkoxyl radical of lactol 27b is formed by an intramolecular addition of the alkoxyl radical generated from the hypoiodite of open-chain alcohol 27a to the carbonyl group as outlined in Scheme 10 (n=5) (vide infra). It should also be noted that no γ-lactone arising from a β-scission of the 10-membered ring was formed. The synthesis of 10-membered lactones, however, may generally be more easily achieved by utilizing 6/6 fused lactols since their equilibrium is entirely towards the lactols in solution.




Scheme 8.

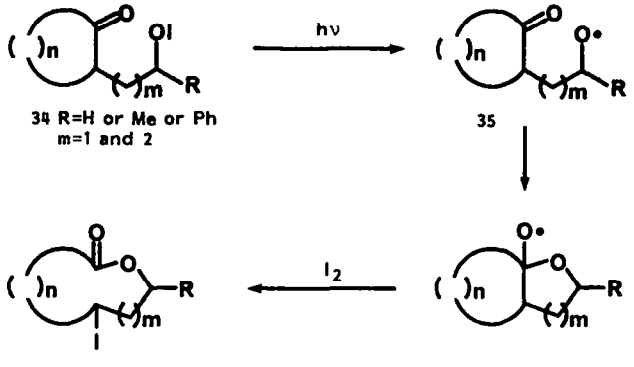
The synthesis of 11-membered lactones (Schemes 9 and 11).

11-Membered lactones may be obtained by the present method through β-scission of any of the 5/8, 6/7, 7/6, or 8/5 fused lactols. Among these lactols, 8/5 and 7/6 fused lactols have been tested for ring expansion. For this purpose a 8/5 fused lactol was newly prepared. The reaction of pyrrolidino-enamine of cyclooctanone with stylene oxide gave two isomeric hydroxyketones, 30a and 31a in a ratio of 1:1.5, which were separable by column chromatography. In contrast to the results for hydroxyketone 27a, the IR spectrum of the crystals as well as the IR spectrum in solution exhibited strong bands due to the carbonyl groups and indicated that both isomeric lactols (30b) and (31b) are in equilibria with its ring-opened forms 30a and 31a in the crystals as well as in solution. The $^1$H NMR spectra of 30a in $CDCl_3$ (90 MHz) then exhibited a multiplet at δ 2.77-3.15 and a doublet of a doublet at δ 4.60 (J=9.1 and 3.8 Hz), assignable to a methine proton adjacent to the carbonyl and to a benzylic proton. The isomer 31a similarly exhibited a multiplet at δ 2.58-2.95 and a doublet of a doublet at δ 4.51 (J=9.0 and 5.0 Hz). Virtually no signals assignable to a benzylic proton of lactol form 30b or 31b were observed in the spectra of either isomers. Since the ratio of the signal due to the benzylic proton to that of the methine proton adjacent to the carbonyl in the spectra of 30a and 31a was approximately 1 to 1, the equilibria between 30a and 30b as well as 31a and 31b were almost entirely towards the hydroxyketones 30a and 31a.




30a 31b 30b 31b 32 cis:trans or trans:cis (2.5:1) 33

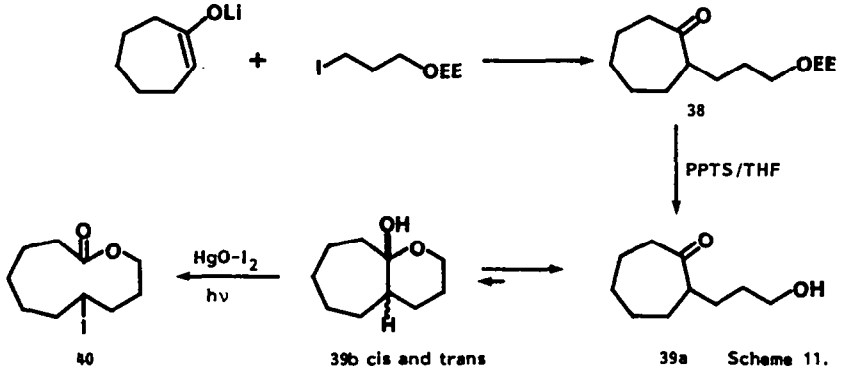
Scheme 9.




34 R=H or Me or Ph m=1 and 2 35 37 36

Scheme 10.

Each hydroxyketone 30a or 31a was then subjected to the ring expansion method described above. To our surprise, each hydroxyketone gave a mixture of cis and trans 11-membered lactone 32 in 65% yields together with α-(2-oxocyclooctyl)-acetophenone (33) in 24% yields. The ratio of the isomers in lactone 32 was 1:2.5 although we were unable to assign which was cis or which was trans. Since the 8/5 fused lactol is almost entirely in a ring-opened form, we suppose that the formation of 11-membered lactone 32 in a rather high yield is formed via alkoxyl radicals 36 corresponding to catacondensed lactols 30b and 31b (Scheme 9); lactone 32 may be generated by an intramolecular attack of the alkoxyl radicals 35 generated from the hypoiodites 34 of hydroxyketones 30a or 31a through a 5-membered transition state as outlined in Scheme 10. Other explanations, however, are possible, as in the case of lactone 28 from a 7/5 fused lactol 27b (vide supra).




40 39b cis and trans 39a Scheme 11.

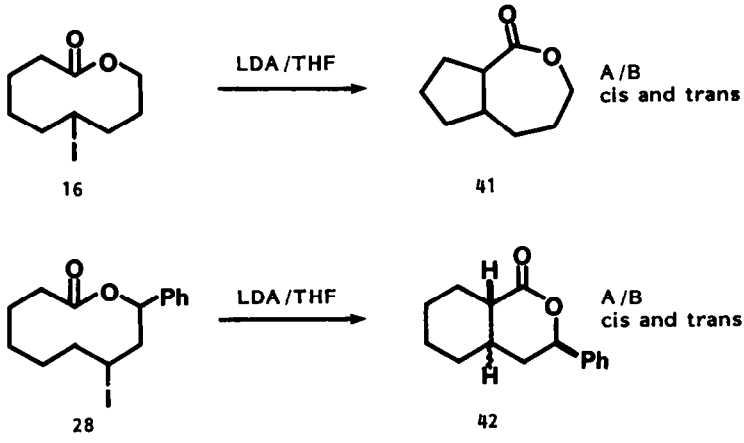
We then attempted to prepare a 7/6 fused lactol. The reaction of cycloheptanone trimethylsilyl enol ether with methyllithium gave the corresponding lithium enolate (Scheme 11). The reaction of the enolate with 1-iodo-3-(1-ethoxy-ethoxy)propane gave α-alkylcycloheptanone (77%). The removal of the protecting group gave the corresponding hydroxyketone 39a.[8] The $^1$H NMR (270 MHz) and IR spectra exhibited that the lactol (a mixture of cis and trans isomers) 39b is in an equilibrium with its ring-opened form 39a in $CDCl_3$ and that the ratio of 39b to 39a is approximately 1:2.8. The two forms 39a and 39b can be separated on TLC silica gel plates, although both forms rapidly equilibrate in solutions.

The photolysis of the lactol 39a in an equilibrium with hydroxyketone 39b in benzene in the presence of mercury(II) oxide and iodine led to the formation of an 11-membered lactone 7-iododecanolide (40) in an unexpectedly high yield (38%) together with the recovered hydroxyketone 39a in a 34% yield.

Transannular cyclizaion of the 10-membered iodolactones, 16 and 28 (Scheme 12).

We then examined the base-catalyzed transannular cyclization of the two 10-membered iodolactones 16 and 28 derived from the 6/6 and 7/5 fused lactol[5]. The treatment of iodolactone 16 in THF-HMPA with LDA at -60°C for 2 h gave a mixture of cis- and trans-2-oxabicyclo[5.3.0]decan-1-one (41) (86%); these were separable by means of TLC. High resolution mass spectra indicated that the molecular formulae of both isomers was $C_9H_{14}O_2$. The IR and $^1H$ NMR spectra indicated that both were stereoisomers of bicyclic ε-lactones 41.

The treatment of iodolactone 28 in THF with LDA at -78°C for 2 h similarly gave a mixture of cis and trans-3β-phenyl-2-oxabicyclo[4.4.0]decan-1-one (42) in a 47% yield. The crystalline mixture was not separable into components, although the MS, IR, and $^1H$ NMR spectra of the mixture were in accord with the assigned structure.




Scheme 12.

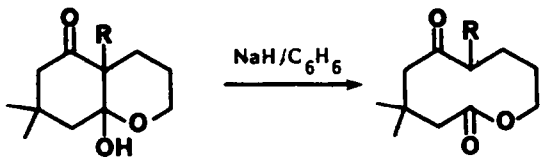
## Conclusions

The foregoing experiments have shown that the method described in this paper may be applied to a facile synthesis of at least 9 to 11-membered lactones and may have a potential for application to the synthesis of smaller and larger ring lactones from cyclic ketones as the readily available starting materials.

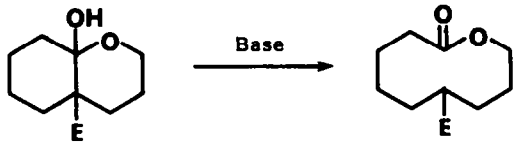
As we noted at the outset of this paper, most of the previous syntheses of medium-ring lactones via the cleavage of the bridged bond of bicyclic compounds have utilized ionic cleavage by strong bases or oxidizing reagents. 10-Membered lactones were thus prepared by a retro Dieckman condensation of bicyclic lactols[7g,j] (Scheme 1). Several groups of chemists have also reported the preparation of medium-ring lactones by means of base-catalyzed fragmentation[7i,k,l,16e,d] of catacondensed lactols with an electron-withdrawing group such as nitro, phenylsulphonyl etc. at their angular carbon (Scheme 14).

In contrast to these methods, the method described in this paper may be carried out in virtually neutral conditions and no extra functional groups necessary for the cleavage are required in the starting catacondensed lactols. The iodine substituent formed after the ring expansion can be used as a functional group for a further transformation or can readily be removed.

The present method thus could replace or compliment some of the previous procedures used for synthesizing the medium-sized lactones.




Scheme 13.




$E=NO_2$, $PhSO_2$, etc.

Scheme 14.

## EXPERIMENTAL

General Methods.

For the instruments used and the general procedure adopted for the photolysis, see Reference 9.

Preparation of 2-(2-Hydroxypropyl)cyclohexanone (1a).

This compound (a mixture of two isomers ) was prepared according to the method used by Britten et al.[11] The $^1H$ NMR in $CDCl_3$ (90 MHz) exhibited a broad signal centred at δ 3.83 and a diffused sextet centred at δ 4.35 assignable respectively to a proton attached to the carbon carrying a hydroxyl group of 1a and to a proton attached to the carbon carrying an ethereal oxygen of 1b. The ratio of the former to the latter was approximately 1 to 2.

Irradiation of Hypoiodite of 2-(2-Hydroxypropyl)cyclohexanone (1a).

To the solution of the catacondensed lactol 1a (200 mg) in dry benzene (64 ml) containing pyridine (0.5 ml), mercury(II) oxide (554 mg) and iodine (650 mg) were added. The solution in a Pyrex vessel was flushed with nitrogen and irradiated with a 100-W high pressure Hg arc for 4 h. The solution was filtered and the filtrate was worked up in the usual manner to give a crude oily product (380 mg). This product was subjected to preparative TLC with a 10:1 mixture of benzene-diethyl ether to yield two fractions A and B in the order of decreasing mobility. Fraction A (192 mg) was a 1:3.5 mixture of two 9-membered iodolactones 5 isomeric with regard to their configurations of the methyl and the iodine substituents: oil; IR (neat) 1728 $cm^{-1}$ (C=O); $^1H$ NMR δ 1.25 (d, J 6.37 Hz, Me), 1.31 (d, J 5.94, Me of the isomer), 4.21-4.53 (1H, m, >CHI), 4.87 (0.78H, m, $-OC\underline{H}CH_3$ of one isomer), 5.12 (0.22H, m, $-OC\underline{H}CH_3$ of another isomer); MS (EI), m/z (%) 282 ($M^+$, 0.6), 155 ($M^+$-I, 100), 95 (56) 55 (98); HRMS (high resolution mass spectrometry). (Found: 282.0103. Calcd for $C_9H_{15}IO_2$: 282.0114). Fraction B (37 mg) was a mixture of two stereoisomeric 5-membered lactones 8: IR (neat) 1763, 1181, 962 $cm^{-1}$; $^1H$ NMR δ 1.37 and 1.42 (each d, J 6.37) and 6.16 Hz, Me of the two isomers), 3.20 (2H, t, J 6.59 Hz, $CH_2I$ of the two isomers), 4.36-4.77 (1H, m, $CH_3CH$-O- of the two isomers); MS (EI), m/z (%) 282 ($M^+$, 4), 155 ($M^+$-I, 100).

Preparation of 2-(2-Hydroxy-2-phenylethyl)cyclohexanone (1b).

This compound (a mixture of two isomers ) was prepared according to ths method used by Britten et al.[11] The $^1H$ NMR in $CDCl_3$ (90 MHz) exhibited a quintet centred at δ 4.84 and a doublet of a doublet at δ 5,22 (J 9.23 and 6.81 Hz) assignable respectively to a proton attached to the carbon carrying a hydroxyl group of 2a and to a proton attached to the carbon carrying an ethereal oxygen of 2b. The ratio of the former to the latter was approximately 1:2.2.

Irradiation of Hypoiodite of 2-(2-Hydroxy-2-phenylethyl)cyclohexanone (1b).

To the catacondensed lactol (150 mg) in dry benzene (37 ml) containing pyridine (0.5 ml) was added mercury(II) oxide (320 mg) and iodine (376 mg). The solution was irradiated for 3 h while being stirred and worked up by the usual method to give a crude oily product. This was subjected to preparative TLC with benzene to yield four fractions. The most mobile fraction was a 9-membered lactone 6 (131 mg); this was a 6:1 mixture of two isomers with regard to the configurations of the phenyl and the iodine substituents: mp 58-64°C; IR 1726 $cm^{-1}$ (C=O); $^1H$ MNR δ 4.35-4.62 (1H, m, CHI of the two isomers), 5.71 (0.86H, dd, J 10.4 and 1.4Hz, $CHC_6H_5$-O- of one isomer), 6.03 (0.14H, dd, J 7.3 and 2.7 Hz, $CHC_6H_5$ of another isomer); MS, m/z (%) 344 ($M^+$, 0.7), 217 ($M^+$-I, 65); HRMS (Found: 344.0269. Calcd for $C_{14}H_{17}IO_2$: 344.0271). The second mobile fraction was a five-membered lactone 9 (11 mg): oil; IR (neat) 1765 (C=O), 1174 $cm^{-1}$; $^1H$ NMR (90 MHz) δ 3.19 (2H, t, J 6.59 Hz, $CH_2I$), 5.56 (1H, t, J 6.05 Hz, CHPh), 7.34 (5H, br.s, $C_6H_5$); MS, m/z (%) 344 ($M^+$, 9), 217 ($M^+$-I, 13), 110 (68), 91 (100); HRMS (Found: 344.0276. Calcd for $C_{14}H_{17}IO_2$: 344. 0272 ). The third mobile fraction was a 5-membered lactone (17 mg) which was the isomer of the above mentioned 5-membered lactone (17 mg): oil; IR (neat) 1764 (C=O), 1161 $cm^{-1}$; $^1H$ NMR δ 3.20 (2H, t, J 6.59 Hz, $CH_2I$), 5.36 (1H, dd, J 10.44 and 5.38 Hz, CHPh), 7.35 (5H, br.s, $C_6H_5$); MS, m/z (%) 344 ($M^+$, 18), 217 ($M^+$-I, 31), 91 (100); HRMS (Found: 344.0272. Calcd for $C_{14}H_{17}IO_2$: 344.0272). The least mobile fraction was α-(2-oxocyclohexyl)acetophenone[11] (11) (16 mg) which was identified by a comparison with a specimen obtained by oxidation of acetal 1b with pyridinium chlorochromate: IR (neat) 1705 (C=O), 1680 ($COC_6H_5$), 1231, 1130, 1002 $cm^{-1}$; $^1H$ NMR δ 2.67 (1H, dd, J 17.14 and 5.27 Hz, $-CH_2COPh$), 3.61 (1H, dd, J 17.14 and 6.37 Hz, $-CH_2COPh$), 3.12 (1H, m, -COCH-).

Preparation of 1-Iodo-3-(1-ethoxyethoxy)propane.

To a solution of 3-iodopropanol (5.4 g), prepared from a commercially available 3-bromopropanol and sodium iodide in dichloromethane (60 ml) containing pyridinium p-toluenesulphonate (250 mg) was added dropwise ethyl vinyl ether in dichloromethane (15 ml) at room temperature. The solution was stirred for 3 h at room temperature. The solution was then washed with water and dried over anhydrous sodium sulphate. Concentration of the reaction mixture gave a crude product which was purified by distillation to yield a pure specimen (6.6 g): bp 49-50°C (0.9 mm Hg); IR (neat) 1125, 1085, 1058, 951 $cm^{-1}$; $^1H$ NMR (90 MHz) δ 1.21 (3H, t, J 7.03 Hz, $OCH_2\underline{CH_3}$), 1.31 (3H, d, J 5.38 Hz, $-CHC\underline{H_3}$), 2.05 (2H, qi, J 6.6 Hz, $-CH_3$), 3.29 (2H, t, J 6.8 Hz, $-CH_2I$), 3.3-3.76 (4H, m, $-CH_2O-$), 4.68 (1H, q, J 5.3 Hz, $-OCHCH_3$).

Preparation of 1-Iodo-3-(1-ethoxyethoxy)butane.

To a solution of 1-iodo-3-butanol[23] (4.5 g), in dichloromethane (50 ml) containing pyridinium p-toluenesulphonate (200 mg) was added dropwise a solution of ethyl vinyl ether (3.5 g) in dichloromethane (15 ml) at room temperature in the course of 30 min. The solution was stirred for 5 h at room temperature. After the usual work-up the crude product obtained was purified by distillation to give a pure specimen (5.1 g): bp 49-50°C (0.4 mm Hg); IR (neat) 1192, 1123, 1092, 1059, 962 $cm^{-1}$ $^1H$ NMR (90 MHz) δ 1.1-1.33 (9H, m, Me), 3.15-3.87 (3H, m, $-OCH_2-$ and -OCH-), 4.65-4.83 (1H, m, -OCHO); MS (EI), m/z (%) 272 ($M^+$, 0.6), 257 ($M^+$-Me, 4.3), 73 (100).

Preparation of 2-[3-(1-Ethoxyethoxy)propyl]cyclohexanone (14).

To a solution of cyclohexanone trimethylsilyl enol ether (12) (300 mg) in dry dimethoxyethane (3 ml) kept at -20°C was added dropwise methyllithium (2.43 ml of a 0.8M solution in diethyl ether) in the course of 15 min. The mixture was stirred for 1 h. After removal of the solvent under vacuum, dry tetrahydrofuran (THF) (2.5 ml) and hexamethylphosphoramide (HMPA) (2.5 ml) was added to the residue. To this mixture 1-iodo-3-(1-ethoxyethoxy)propane (455 mg) was added over a 30 min at -20°C. The solution was stirred at room temperature for 10 h. The reaction mixture was

then diluted with water, extracted with diethyl ether, and dried over anhydrous sodium sulphate. The usual work-up gave an oily product. The product was purified by preparative TLC to give a pure 2-substituted cyclohexanone 14 (210 mg): oil; IR (neat) 1708 $cm^{-1}$ (C-O); $^1H$ NMR (90 MHz) δ 1.19 (3H, t, J 5.94 Hz, $-CH_2\underline{CH}_3$), 1.29 (3H, d, J 5.27 Hz, $-CHCH_3$), 3.20-3.74 (2H, m, $-OCH_2-$), 4.66 (1H, d, J 5.27 Hz, $OCH_2O-$); MS (EI), m/z (%) 155 (16.2), 139 (77), 73 ($CH_3C{=}\overset{+}{O}C_2H_5$, 100).

Preparation of 1-Oxadecalin-9-ol (15).

To a solution of 14 (90 mg) in acetone (7 ml) was added dropwise a 1:1 mixture of acetic acid and water (2 ml) at room temperature. The solution was stirred for 2 days and extracted with diethyl ether. The ethereal solution was washed successively with a 5% sodium hydrogencarbonate solution, water and brine, and then dried over anhydrous sodium sulphate. Concentration of the solution left crystals which were subjected to preparative TLC with a 1:1 mixture of hexane-diethyl ether to yield pure 1-oxadecalin-9-ol (15) (57 mg).[8]

Irradiation of Hypoiodite of 1-Oxadecalin-9-ol (15).

To a solution of the catacondensed lactol 15 (200 mg) in dry benzene (64 ml) containing pyridine (0.5 ml) was added mercury(II) oxide (554 mg) and iodine (650 mg). The solution was irradiated for 3 h while being stirred and worked up by the usual method to give an oily product which was subjected to preparative TLC with benzene to yield a pure 10-membered lactone 16 (284 mg): oil; IR (neat) 1726 (C=O), 1253, 1230, 1025 $cm^{-1}$; $^1H$ NMR (90 MHz) δ 3.73-4.00 (1H, m, $-CH_2O-$), 4.56-4.84 (2H, m, $-CH_2O-$ and $-CHI-$); MS (EI), m/z (%) 155 ($M^+$-I, 100). HRMS (Found: 155.1076. Calcd for $C_9H_{15}O_2I^+$-I: 155.1071).

Preparation of 2-[3-(1-Ethoxyethoxy)butyl]cyclohexanone (17).

To a solution of cyclohexanone trimethylsilyl enol ether (12) (1.0 g) in dry dimethoxyethane (10 ml) kept at -20°C was added dropwise methyllithium over 15 min (10.5 ml or a 0.58 M solution in diethyl ether). The mixture was stirred at -20°C for 1 h. After the removal of the solvent under vacuum, a 1:1 mixture of THF-HMPA (20 ml) was added to the residue. 1-Iodo-3-(1-ethoxyethoxy)butane (1.6 g) was then added to the solution in the course of 30 min at -20°C. The solution was stirred at room temperature for 20 h. The reaction mixture was diluted with water and extracted with diethyl ether and dried over anhydrous sodium sulphate. The usual work-up gave an oily product (1.6 g) which was purified by preparative TLC with a 3:1 mixture of hexane-diethyl ether to give a pure specimen (597 mg): oil; IR (neat) 1709 (C=O), 1132, 1086, 1060 $cm^{-1}$; $^1H$ NMR (90 MHz) δ 1.08-1.32 (6H, m, Me), 3.25-3.79 (3H, m, $-CH_2O-$ and $>CHO-$), 4.58-4.81 [1H, m, $-OCH(CH_3)O-$]; MS (EI) m/z (%) 153 (74), 73 ($C_4H_9O^+$, 100).

Preparation of cis and trans-1-Oxa-r-2-methyl-t-9-decalinols (18).[22]

To a solution of 2-substituted cyclohexanone 17 (540 mg) in acetone (40 ml) was added dropwise a 1:1 mixture of acetic acid and water (12 ml) at room temperature. The solution was stirred for 24 h and extracted with diethyl ether. The ethereal solution was washed successively with a 5% sodium hydrogen carbonate solution, water and brine, and dried over anhydrous sodium sulphate. The usual work-up gave crystals which were subjected to preparative TLC with a 1:1 mixture of hexane-diethyl ether to yield two fractions. The more mobile fraction was pure trans-1-oxa-r-2-methyl-t-9-decalinol (18b) (164 mg) which was recrystallized from petroleum ether: mp 80-82°C; IR 3407 $cm^{-1}$ (OH); $^1H$ NMR (90 MHz) δ 1.13 (3H, d, J 6.16 Hz, Me), 3.90-4.25 (1H, m, $OC\underline{H}CH_3$); MS (EI), m/z (%) 170 ($M^+$, 25), 152 ($M^+-H_2O$, 62), 98 (100). (Found: C, 70.37; H, 10.55. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66). The less mobile fraction was cis-1-oxa-r-2-methyl-t-9-decalinol (18a) (135 mg) which was also recrystallized from petroleum ether: mp 108-110°C; IR 3270, 1083, 970 $cm^{-1}$; $^1H$ NMR (90 MHz) δ 1.14 (3H, d, J 6.16 Hz, Me), 3.40-3.80 (m, $-OCHCH_3$ of

the ring-opened alcohol), 3.92-4.23 (1H, m, $-OCHCH_3$ of the lactol form); MS, m/z (%) 170 ($M^+$, 8), 152 ($M^+-H_2O$, 100). Found: C, 70.33; H, 10.52. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66).

Irradiation of Hypoiodite of trans-1-Oxa-r-2-methyl-t-9-decalinol (18b).

To a solution of trans-1-oxa-9-decalinol (18a) (100 mg) in dry benzene (35 ml) containing pyridine (300 mg) were added mercury(II) oxide (254 mg) and iodine (300 mg). The solution was irradiated for 2 h and worked up by the usual method to give an oily product (180 mg) which was purified by preparative TLC with benzene to yield pure 6-iododecan-9-olide (19) (150 mg): oil; IR (neat) 1721 (C=O), 1256, 1229, 1035 $cm^{-1}$; $^1H$ NMR (90 MHz) $\delta$ 1.29 (3H, d, J 6.81 Hz, Me), 4.46-4.74 (1H, m, -CHI), 4.93-5.24 (1H, m, $-OCHCH_3$); MS (EI), m/z (%) 169 ($M^+$-I, 69), 78 (100); HRMS. (Found: 169.1232. Calcd for $C_{10}H_{17}IO_2$-I: 169.1229).

Photolysis of Hypoiodite of cis-1-oxa-r-2-methyl-t-9-decalinol (18a) in the Presence of Mercury(II) Oxide and Iodine.

To a solution of the cis-1-oxa-2-methyl-9-decalinol (18a) (100 mg) in dry benzene (35 ml) containing pyridine (0.25 ml) were added mercury(II) oxide (254 mg) and iodine (300 mg). The solution was irradiated for 3 h and worked up as described above to yield a 1:1 mixture of cis and trans 10-membered iodolactones 19 (132 mg): oil; IR (neat) 1725 $cm^{-1}$; $^1H$ NMR $\delta$ 1.27 and 1.28 (each d, J 6.37 and 6.81 Hz, Me of the cis- and trans-isomers), 4.03-4.34 and 4.43-4.75 (each m, -CHI of cis- and trans-isomers), 4.85-5.24 (m, $-OCHCH_3$ of cis- and trans-isomers).

Preparation of (±)-Phoracantholide I (20).

To a solution of the iodo lactone 19 (100 mg) in dry benzene (5 ml) was added dropwise tributyltin hydride (150 mg) at room temperature under a nitrogen atmosphere. The solution was stirred for 3 h and concentrated to give a crude oily product. This was twice purified by preparative TLC with benzene to yield a pure Phoracantholide I (47 mg). Its spectral data were in agreement with those published for this natural product.[16]

Irradiation of Hypoiodite of a Mixture of 5α- and 5β-4-Oxacholestan-5-ols (21).[18]

To a solution of hemiacetal 21 (200 mg) containing pyridine (0.2 ml) was added mercury(II) oxide (222 mg) and iodine (260 mg). The solution was irradiated for 2.5 h while being stirred and worked up by the usual method to give an oily product. This was subjected to preparative TLC with a 1:1 mixture of benzene-hexane to yield two fractions. The more mobile fraction was ring-expanded (Z)-lactone 22 (55 mg), which was recrystallized from methanol: mp 61-63°C; IR 1719 (C=O), 1263, 1235, 1040 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 0.70 (3H, s, 18-H), 1.67 (3H, s, 19-H), 3.63 (1H, dd, J 13.55, 10.62, and 2.93 Hz, 3-H), 4.61 (1H, dd, J 10.62 and 4.40 Hz, 3-H), 5.20 (1H, ddd, J 10.62, 6.23, and 1.10 Hz, 1-H); MS, m/z (%) 388 ($M^+$, 42), 275 (66), 94 (100). (Found: C, 80.25; H, 11.50. Calcd for $C_{26}H_{44}O_2$: C, 80.35; H. 11.41. The less mobile fraction was ring-expanded (E)-lactone 23 (135 mg), which was recrystallized from methanol: mp 61-63°C; IR 1732 (C=O), 1163, 1126, 1107, 1030, 983 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 0.71 (3H, s, 18-H), 1.63 (3H, s, 19-H), 4.01 (1H, dd, J 10.44 and 7.15 Hz, 3-H), 4.91 (1H, ddd, J 11.72, 10.44, and 4.76 Hz, 3-H), 5.07 (1H, ddd, J 11.36, 5.13, and 1.10 Hz, 1-H); MS m/z (%) 388 ($M^+$, 50), 275 (62), 94 (100). (Found: C, 80.25; H, 11.38. Calcd for $C_{26}H_{44}O_2$: C, 80.35; H, 11.41).

2-(2-Hydroxy-2-phenylethyl)cycloheptanone.

This compound was prepared according to the procedure of Britten et al.[11] $^1H$ NMR ($CDCl_3$) (270 MHz) $\delta$ 4.69 (0.2H, quintet, J 4.4 Hz, benzylic proton of 27a), 5.02 (0.08H, dd, J 5.5 and 10.3 Hz, benzylic proton of 27b), 5.15 (0.72H, dd, J 5.5 and 10.3 Hz, benzylic proton of isomeric 27b).

Photolysis of Hypoiodite of 2-(2-Hydroxy-2-phenylethyl)cycloheptanone (27a) in the

Presence of Mercury(II) Oxide and Iodine.

To the hemiacetal 27b (150 mg) in dry benzene (35 ml) containing pyridine (0.4 ml), mercury(II) oxide (452 mg) and iodine (529 mg) were added. The solution was irradiated for 4 h while being stirred and worked up by the usual method to give a crude oily product. This was subjected to preparative TLC with a 20:1 mixture of benzene-diethyl ether to yield two fractions A and B in decreasing mobility. Fraction A (190 mg) was a 1:1.8 mixture of isomeric 10-membered iodolactones: mp 95-97°C; IR 1723 (CO), 1268, 1164, 1045 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (90 MHz) δ 4.20-4.48 (1H, m, -CHI), 5.73 (0.64H, dd, J 10.33 and 2.41 Hz, -CHPh), 5.95 (0.36H, t, J 3.85 Hz, -CHPh), 7.31 (5H, br.s, aromatic H); MS m/z (%) 358 ($M^+$, 0.2), 231 ($M^+$-I, 55.9), 117 (81.0), 55 (100). (Found: C, 50.21; H, 5.34; I, 35.37. Calcd for $C_{15}H_{19}IO_2$: C, 50.29; H, 5.35; I, 35.43. Fraction B was α-2-oxocycloheptylacetophenone (14 mg): IR 1700 (C=O), 1681 ($C_6H_5CO$), 1207 $cm^{-1}$; $^1H$ NMR δ 2.87 (1H, dd, J 16.92 and 4.40 Hz, $-CH_2COC_6H_5$), 3.22-3.48 (1H, m, -COCH-), 7.25-8.01 (5H, m, aromatic H); MS m/z (%) 230 ($M^+$, 10.6), 120 (34.3), 105 ($\overset{+}{O}$≡CPh, 100).

Preparation of 2-(2-Hydroxy-2-phenyl)cyclooctanone (30a) and (31a).

The enamine of cyclooctanone was prepared by refluxing a solution of cyclooctanone (1.5 g), pyrrolidine (3.0 g) and p-toluensulphonic acid (10 mg) in benzene (5 ml) in a Dean-Stark apparatus for 5 h. The solvent and pyrrolidine was evaporated to give an oily enamine which was used without further purification. To a solution of the above 1-pyrrolidino-1-cyclooctene[24] in dimethyl formamide (10 ml) styrene oxide (3.8 g) was added and the solution was heated under reflux for 4 h. The reaction mixture was cooled to room temperature and water (3 ml) was added. The solution was again heated under reflux for 1 h. The usual work-up of the reaction mixture gave crude products which were subjected to column chromatography with silica gel (Merck, silica gel 60, 70-230 mesh, 100 g). Elutions with a 5:1 mixture of benzene-ethyl acetate gave two fractions. The first fraction was a 2-(2-hydroxy-2-phenylethyl)cyclooctanone: mp 72-78°C; IR (Nujol) 3450 (OH), 3330 (OH), 1696 (C=O), 1061, 1027, 947, 935 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (90 MHz) δ 2.77-3.15 (1H, m, -COCH-), 4.60 (1H, dd, J 9.1 and 3.8 Hz, benzylic H), 7.27 (5H, s, aromatic H); MS m/z (%) 246 ($M^+$, 3.3), 228 ($M^+-H_2O$, 16.4), 126 (65.2), 98 (100). (Found: C, 77.89; H, 8.97. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. The second fraction was the isomeric 2-alkylcyclooctanone: mp 80-90°C; IR (Nujol) 3400 (OH), 1684 (C=O), 1205, 1095, 1062, 968 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (90 MHz) δ 2.58-2.95 (1H, m, -COCH-), 4.61 (1H, dd, J 9.0 and 5.0 Hz, benzylic H), 7.27 (5H, s, aromatic H); MS, m/z (%) 246 ($M^+$, 3.8), 228 ($M^+-H_2O$, 33.8), 98 (100). (Found: C, 78.00; H, 8.85. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00).

Photolysis of Hypoiodite of 2-(2-Hydroxy-2-phenyl)cyclooctanone (30a) in the Presence of Mercury(II) Oxide and Iodine.

To the hemiacetal 30a (60 mg) in dry benzene (14 mg) containing pyridine (215 mg), mercury(II) oxide (159 mg) and iodine (212 mg) were added. The solution was subjected to the photolysis (4.5 h) and worked up by the usual method to give a crude oily product. This was subjected to preparative TLC to yield two fractions A and B in an order of decreasing mobility. Fraction A (59 mg) was 11-membered iodolactone 32: mp 131-136°C; IR (Nujol) 1709 (C=O), 1260, 1243, 1162, 1010 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (90 MHz) δ 4.40-4.66 (1H, m, -CHI), 5.78 (0.71H, dd, J 10.00 and 1.65 Hz, benzylic H), 6.01 (0.29H, dd, J 8.46 and 2.53 Hz, benzylic H), 7.30 (5H, br.s, aromatic H); 7.30 (5H, br.s, aromatic H) ; MS m/z (%) 245 ($M^+$-I, 40.8), 117 (100). (Found: C, 51.52; H, 5.66; I, 34.07. Calcd for $C_{16}H_{21}IO_2$: C, 51.63, H, 5.69; I, 34.09). Fraction B (14 mg) was α-(2-oxocyclooctyl)acetophenone: mp 71-72°C; IR (Nujol) 1692 (C=O), 1682 ($-COH_6H_5$), 1276, 1212, 1000, 856, 765 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 2.13-3.80 (5H, m, $-CH_2COCH-CH_2CO-$), 7.28-7.96 (5H, m, aromatic H); MS m/z (%) 244 ($M^+$, 7.7), 105 (100), 77 (38.7). (Found: C, 78.89; H, 8.19. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25.

Photolysis of Hypoiodite of the Isomer of 2-(2-Hydroxy-2-phenyl)cyclooctanone (31b).

The isomeric lactol (31b) was irradiated in a manner similar to that used for lactol (30b). The result was nearly the same as with the isomer (30b).

Preparation of 2-[3-(1-Ethoxyethoxy)propane]cycloheptanone (38).

To a solution of trimethylsiloxy-1-cycloheptene (500 mg) in dry dimethoxyethane (5 ml) kept at -20°C was added dropwise methyllithium (4.8 ml of a 0.58 M solution in diethyl ether). The mixture was stirred at -20°C for 1 h. After the removal of the solvent under vacuum, the residue was dissolved in dry THF (4 ml) and HMPA (4 ml). 1-Iodo-3-(1-ethoxyethoxy)-propane (700 mg) was then added to the solution over a 10 min at -20°C. The solution was stirred at room temperature for 10 h. The usual work-up gave an oily product. It was purified by means of preparative TLC with a 1:1 mixture of hexane-diethyl ether to give a pure 2-substituted cycloheptanone 38 (507 mg) as a liquid. IR (neat) 1704 (C=O), 1134, 1008, and 1061 $cm^{-1}$; $^1H$ NMR $\delta$ 1.19 (3H, t, J 7.03 Hz, $-CH_2\underline{CH_3}$), 1.28 (3H, d, J 5.27 Hz, $CH\underline{CH_3}$), 2.30-2.65 (3H, m, $-\underline{CH_2}COC\underline{H}-$), 3.28-2.73 (4H, m, $2-O\underline{CH_2}-$), 4.65 (1H, q, J 5.49 Hz $-OCH(CH_3)O-$); MS (EI), m/z (%) 197 ($M^+-CH_3\dot{C}H_2O-$, 0.8%), 169 ($M^+-CH_3\dot{C}H_2O{=}CHCH_3$, 18.4), 153 (58.8), and 73 (100).

Preparation of 2-(3-Hydoxypropyl)cycloheptanone (39a).

To a solution of 38 (540 mg) in THF (5 ml), water (0.3 ml) and pyridinium p-toluenesulphonate (50 mg) were added. The solution was stirred for 24 h and extracted with diethyl ether. After the usual work-up, a crude oily product was purified by preparative TLC with a 1:1 mixture of hexane-diethyl ether to give a pure 2-(3-hydroxypropyl)cycloheptanone (39a) (250 mg).[8] $^1H$ NMR (270 MHz) $\delta$ 2.41- 2.57 (m, $C\underline{H_2}COCH$ of 39a), 3.28-3.50 (m, $OCH_2$ of 39b), 3.61 (dt, J 1.84 and 6.23 Hz, $C\underline{H_2}OH$ of 39a) and 3.85 (t, J 5 Hz, $-OCH_2-$ of 39b).

Irradiation of Hypoiodite of 2-(3-Hydroxypropyl)cycloheptanone (39a).

To a solution of the hydroxyketone 39a (60 mg) in dry benzene (18 ml) containing pyridine (0.2 ml) was added mercury(II) oxide (230 mg) and iodine (269 mg). The solution was subjected to the photolysis in the usual manner (4 h). The solution was worked up in the usual manner to give a crude oily product. The product was subjected to preparative TLC with benzene to yield two fractions. The more mobile product (40 mg, 38%) was 7-iododeca-10-olide (40). IR (neat) 1732 (lactonic C=O), 1247, 1172, 1142 1060, 1000, and 948 $cm^{-1}$; $^1H$ NMR $\delta$ 4.16-4.42 (3H, m, $-CH_2OCO$ and CHI); MS m/z (%) 295 ($M^+$-H, 7.8%), 169 ($M^+$-I, 29.5), and 41 (100); HRMS (Found; $M^+$-1, 295.0186. Calcd for $C_{10}H_{16}IO_2$ (M-H), 395.0195. The less mobile fraction (21 mg) was the starting hydroxyketone 31a.

Transannular Cyclization of 10-Membered Iodolactone 16.

To a solution of diisopropylamine (63 ml) in dry THF (2 ml) at -20°C was added dropwise butyllithium (1.55 M in hexane) (0.29 ml) in an atmosphere of nitrogen. After it had been stirred for 30 min, dry hexamethylphospholic amide (HMPA) (0.5 ml) was added to the solution and the solution was cooled to -60°C. Iodolactone 16 (83 mg) in THF (2 ml) was then added dropwise to the mixture and stirred for 2 h. The reaction was quenched by the addition of a saturated ammonium chloride solution and the reaction mixture was extracted with diethyl ether. The ethereal extract was washed with water, dried over anhydrous sodium sulphate and evaporated to give crude lactones. These were subjected to preparative TLC with a 5:1 mixture of benzene-diethyl ether to give two fractions. The more mobile fraction was one of cis- or trans-2-oxabicyclo[5.3.0.]decan-1-one (41) (21 mg) and the less mobile fraction was the isomer (18 mg): IR 1728 (C=O), 1181, 1129, 1090 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (270 MHz) $\delta$ 3.21 (1H, dt, J 11.36 and 8.25 Hz, -COCH-), 4.23 (1H, dd, J 12.46 and 7.32 Hz, $-OCH_2-$), 4.35 (1H, dt, J 12.46 and 4.40 Hz, $-OCH_2-$); MS m/z (%) 154 ($M^+$, 10.4), 113 (44.9), 67 (100); HRMS. (Found: 154.0988. Calcd for $C_9H_{14}O_2$: 15.0993). The isomer: IR 1727 (C=O), 1173, 1078 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (270 MHz) $\delta$ 2.72 (1H, dt, J 10.62 and

8.43 Hz, -COCH-), 4.26-4.31 (2H, m, $-OCH_2-$); MS m/e (%) 154 ($M^+$, 21.1), 95 (55.9), 67 (100); HRMS. (Found: 154.0998. Calcd for $C_9H_{14}O_2$: 154.0993).

Transannular Cyclization of 10-Membered Iodolactone 28.

To a solution of diisopropylamine (31 ml) in dry THF (1.5 ml) at -10°C was added dropwise butyllithium (1.55 M in hexane) (0.14 ml). After it had been stirred for 20 min the solution was cooled to -78°C. Iodolactone 28 (40 mg) in THF (1 ml) was then added to the solution dropwise and stirred for 2 h at-78°C and warmed up to room temperature. The reaction was quenched by the addition of saturated ammonium chloride solution and the reaction mixture was extracted with diethyl ether. The ethereal extract was washed with water, dried over anhydrous sodium sulphate and evaporated to give crude lactones. The products were subjected to preparative TLC with a 10:1 mixture of benzene-diethyl ether to give a mixture of cis- and trans-2-oxa-3β-phenylbicyclo[4.4.0]decan-1-one (42): mp 138-148°C; IR (Nujol) 1717 (C=O), 1706 (C=O), 1168, 1124, 1064, 1008, 765 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) (270 MHz) δ 2.87 (0.33H, br.q, J 5.1 Hz, -COCH-), 5.28 (0.33H, dd, J 12.3 and 3.4 Hz, benzylic H), 5.36 (0.67H, dd, J 11.5 and 3.4 Hz, benzylic H), 7.36 (5H, m, aromatic H); MS m/z (%) 230 ($M^+$, 5.0), 186 ($M^+-CO_2$, 6.2), 104 (100); HRMS (Found: 230.1291. Calcd for $C_{15}H_{18}O_2$: 230.1276).

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