DBU-Catalyzed Deconjugation of 7-Substituted 3,4-Didehydro-2-oxepanones. Deuterium Incorporation, Significance of the Imine Double Bond, and Application to the Synthesis of a Key Pharmacophore

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7-Substituted 3,4-Didehydro-2-oxepanones are conveniently deconjugated to the 4,5-didehydro derivatives by DBU. The isomerization of 7-benzyl-substituted 2-oxepanones proceeds to the extent of 90% over the initial 3 h; the concentration falls gradually thereafter to achieve, in 25 h, a 3:2 equilibrium in favor of deconjugation. Such an equilibrium does not exist for the 7-methyl and the 7-(2-phenethyl) derivatives. The significance of the imine double bond in DBU has been explored. The isomerization in $CDCl_3$ causes deuterium incorporation at positions 3 and 5 of the 2-oxepanones examined and at position 6 of DBU. The mechanistic rationales for these deuterium incorporations are advanced. The transformation of 7-benzyl-3,4-didehydro-2-oxepanone into a bicyclo[3.3.0] skeleton that is present in a diverse class of biologically active natural products is described as a possible potential use of the present deconjugation methodology.

Introduction

In connection with a synthetic program aimed at the study of π-facial selectivity of reactions on 7-ring skeletons, we required sufficient quantities of 7-alkyl-4,5-dehydro-2-oxepanones. We considered isomerization of the related 3,4-didehydro species for their ready availability from the fully saturated 2-oxepanones on introduction of the requisite π bond through the standard selenium methodology. The deconjugation of α,β-unsaturated carbonyl compounds has traditionally been achieved by the use of strong bases such as $(Me_3Si)_2NK$ in THF at −78 °C,[1] LDA in THF/HMPA at −78 °C,[2] lithium *N*-isopropylcyclohexylamide in THF at −78 °C,[3] *t*-BuOK in *t*-BuOH at rt,[4] KNH_2 in liquid NH_3,[5] and KH in THF at 0 °C.[6] The dienolate, so generated, is kinetically quenched with an aqueous acid. These reactions require good handling skills and elaborate reaction setups including inert atmosphere. These bases are expensive as well. Nevertheless, we attempted LDA and KH on 7-benzyl-3,4-didehydro-2-oxepanone using literature protocols. The results were disappointing. Whereas mostly the starting material was recovered from the reaction with LDA, the complex products mixture obtained from KH in THF at 0−30 °C did not contain any of the desired deconjugated species.

Pete and co-workers[7] have studied conjugated γ- and δ-lactones with the unsaturation outside the ring and reported their photodeconjugation in decent yields. Weedon and co-workers[8] have reported the photodeconjugation of acyclic unsaturated esters in the presence of a catalytic amount of a base. 3-Substituted 8-ring enones have also been studied and shown to undergo photoinduced nonregiospecific deconjugation.[9] The photodeconjugation of unsaturated 2-oxepanones appears to be unreported. However, the requirement of the expensive photochemical equipment and the limitations on the reactants' quantity make the photodeconjugation less attractive on a preparative scale. We, therefore, set out to explore alternative economical ways to achieve the desired deconjugation.

We present herein an account of our results on the successful utilization of DBU (and also DBN) for the desired deconjugation of selected 3,4-didehydro-2-oxepanones and the transformation of 7-benzyl-4,5-didehydro-2-oxepanone into a bicyclo[3.3.0] skeleton that is present in a class of natural products possessing diverse biological activity.

Starting Materials

The requisite starting materials **6a**−**e** were prepared as per the sequence given in Scheme 1. 2-Carbomethoxycyclohexanone was subjected to alkylation, decarboxy-

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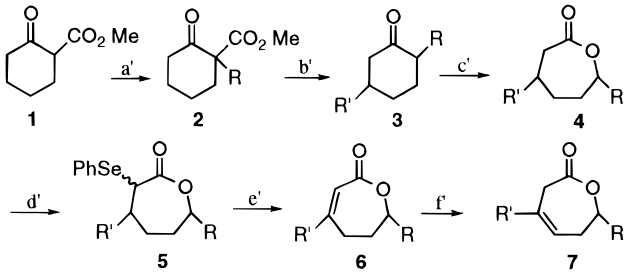
Scheme 1. Syntheses of the 3,4-Didehydro-7-ring Lactones and Their Isomerization to the 4,5-Didehydro Species[a]



a. R = Me, R' = H **b**. R = CH_2Ph, R' = H **c**. R = $CH_2C_6H_4OMe$-*p* , R' = H
d. R = CH_2CH_2Ph, R' = H **e**. R = *iso*-Pr, R' = Me

[a] Reagents: (a′) KF/Al_2O_3, RBr, CH_3CN, rt (for **2b** and **2c**) or NaH, C_6H_6/DMF, NaI, reflux (for **2d**); (b′) LiCl, DMF, reflux; (c′) peracid, $CHCl_3$; (d′) LDA, PhSeBr, THF; (e′) H_2O_2, Py, CH_2Cl_2; (f′) DBU, solvent, rt.

lation,[10] Baeyer−Villiger oxidation,[11] selenenation, and selenoxide elimination,[12] in that order, to make available the requisite **6b**−**d**. The 7-methyl derivative **6a** was prepared from the commercially available 2-methylcyclohexanone (**3**, R = Me, R′ = H) using a similar protocol, commencing from decarboxylation. Likewise, the 7-isopropyl-4-methyl derivative **6e** was prepared from (±)-menthone (**3**, R = *i*-Pr, R′ = Me); the synthesis commenced from Baeyer−Villiger oxidation. The species **3b**,[13] **3c**,[14] **3d**,[15] **4a**,[16] **6a**,[16] and **4e**[16] exhibited known ^{1}H and IR spectral characteristics. The structures of all other intermediates were secured firmly from spectroscopic data and elemental analyses (vide infra). The species **6b**−**e** exhibited vinyl ^{1}H chemical shifts expected of α,*β*-unsaturated carbonyls. The carbonyl IR absorptions were also fully supportive of olefin conjugation. The selenenation reaction furnished, in each instance, a mixture of the two possible isomers of **5** that were not separated because the selenium-containing stereogenic center was soon to be destroyed through selenoxide elimination to generate **6**. DBU and DBN used in the present study were purchased from Fluka and used as received. The $CDCl_3$ used for reaction monitoring by ^{1}H NMR and for the study of deuterium incorporation in oxepanones was 99.8% in deuterium content and was procured from Sigma.

Reaction Monitoring

The transformation of **6** into **7** was monitored by ^{1}H NMR in $CDCl_3$. The characteristic absorptions of the olefinic hydrogens in **6a**−**d** diminished (or disappeared) with time, and a new set of absorption(s) characteristic of the olefinic protons in **7a**−**d** appeared (*vide experimental*). The relative integrals of these absorptions provided information about the extent of conversion. In the reaction of **6e**, a new absorption at *δ* 5.44 (br s) appeared at the expense of an absorption at *δ* 5.86 (t, *J* = 1.2 Hz). In the cases **6b** and **6c**, the reactions were allowed to proceed for 3 h, except to study equilibration, to achieve 90% conversions when they were quenched with dilute aqueous HCl. The preparative-scale isomerizations were carried out in $CHCl_3$ for 3 h for **6b** and **6c** (90% conversion) and for 4 h for **6a** and **6d** (quantitative conversion). The deconjugation of **6e** was too slow to be preparatively useful.

Results and Discussion

1. Deconjugative Isomerization. While exploring the epoxidation of α,*β*-unsaturated carbonyls using *t*-BuOOH and DBU, we isolated, in addition to the expected oxiranes, 4,5-didehydro-7-methyl-2-oxepanone (**7a**)[16] from the reaction of the corresponding 3,4-didehydro species **6a**.[17,18] In an experiment in which *t*-BuOOH was not present, the conversion of **6a** into **7a** was quantitative and complete in 3 h with 1 equiv of DBU. This experiment, therefore, demonstrated DBU as a possible promising base for the deconjugation of 3,4-dehydro-2-oxepanones. We wished to study its scope and, hence, instituted an investigation. The details of our findings are described below.

7-Benzyl-3,4-didehydro-2-oxepanone (**6b**) was reacted with 1 equiv of DBU in $CDCl_3$. There was 90% deconjugation to **7b** in 3 h. Interestingly, in an equilibrium study in $CDCl_3$, a continuous drop in the concentration of **7b** with a corresponding rise in the concentration of **6b** was noticed after the initial 3 h. A 2:3 ratio of **6b**:**7b** was achieved in 25 h. The observation that this ratio did not change afterward suggests the above to have constituted the equilibrium point.

The above 2:3 equilibrium composition is indicative of a small energy difference between **6b** and **7b**. The observation that the deconjugated species is more abundant than the conjugated counterpart is to show the diminished effectiveness of conjugation between the carbonyl and the double bond in medium ring lactones than the conjugation in the small ring systems. Whitham[19] and Hirsch[20] have made similar observations and advanced a rationale. In a reaction with only a catalytic amount of DBU (10 mol %) in Al_2O_3-filtered $CDCl_3$, 90% deconjugation took place in 100 h; sustained exposure caused a slow reversal of the reaction. Further, in an experiment in which **7b** was allowed to stand with 10 mol % DBU in Al_2O_3-filtered $CDCl_3$, the formation of **6b** was detected by ^{1}H NMR after 60 h. The same reaction with 1 equiv of DBU was much faster, and the equilibrium **6b**:**7b** = 2:3 was established in 50 h. The related

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Table 1. Deconjugative Isomerizationof the 7-Ring Lactone Species 6 into 7[a]

substrate	time (h)	conversion[b] (%)	yields[c] (%)	equil time[d] (h)	equil ratio[e] (**6**:**7**)
6a	03	100	quant	no equil	
6b	03	>90	90	25	2:3
6c	03	>90	90	25	2:3
6d	03	100	quant	no equil	
6e	24	20	18	na	

[a] All the reactions were conducted in $CHCl_3$ on a 0.05 mmol scale. [b] Deduced from ^1H spectral integrals of the characteristic signals. [c] The actual isolated yields based on the total conjugated lactone taken. [d] There was no observable change in the ratio after the indicated time. [e] Calculated from ^1H integrals of the products mix after aqueous acidic workup.

7-(*p*-methoxybenzyl) derivative **6c** behaved in a similar fashion. There was 90% deconjugation with 1 equiv of DBU in the first 3 h; the reversal began thereafter to attain **6c**:**7c** = 2:3 equilibrium in 25 h.

We have also treated the 7-(2-phenethyl) derivative **6d** with DBU in $CDCl_3$ under similar conditions. Interestingly, the only product obtained (**7d**) even after 50 h was that of deconjugation. This behavior is similar to that of the 7-methyl analogue **6a**. All the results on isomerization have been collected in Table1 for a convenient comparison. The difference in the behavior of the 7-methyl and the 7-benzyl species in regard to the onset of equilibrium is not understood.

2. Deuterium Incorporation. From each of the isomerization experiments with **6a**−**d** in $CDCl_3$ there was observed a prominent enhancement in the ^1H signal for $CHCl_3$. This led us to critically examine the lactones **6b** and **7b** obtained from a full equilibration experiment for a possible deuterium incorporation. From a combination of ^1H and ^1H-decoupled ^{13}C NMR spectra, partial deuterium incorporation at positions 3 and 5 was deduced. While the absorptions for protons on positions 3 (δ 5.99−5.95, dd, J = 12, 1.5 Hz) and 5 (δ 2.54−2.26, m) in **6b** integrated less than the requisite one and two protons in **6b**, respectively, the ^{13}C spectrum showed two triplets centered at δ 122.31 (C3) and 31.15 (C5). These carbons in the undeuterated species absorb at δ 122.27 and 31.24, respectively. From the relative integrals, the level of deuterium incorporation at both positions was computed at 38−40%. The same set of NMR spectra of **7b** were similarly instructive. The absorptions of the vinyl proton on C5 (δ 5.69−5.61, m) and that of one proton on C3 (δ 3.07−2.99, dd, J = 16.5 and 8.7 Hz) integrated less than the requisite one full proton each. The extent of deuterium incorporation was calculated, once again, to be 38−40% from the relative integrals. Interestingly, the other proton at C3 (δ 3.64, bd, J = 16.5 Hz) in **7b** integrated one full proton. This is of conformational significance. Presumably, only the C3−H that is nearly orthogonal to the σ-plane of the double bond in the chairlike conformation must have undergone the exchange. These findings were confirmed further from the $^{13}C-D$ splittings; while a triplet centered at δ 34.87 (δ 34.98 in the nondeuterated material) for C3 indicated only one deuterium atom on it, another triplet centered at δ 118.6 (δ 118.7 in the nondeuterated material) for C5 confirmed the deuterium incorporation at this position as well.

To investigate the possible course of deuterium incorporation, DBU was mixed with $CDCl_3$ and the ^1H spectra recorded at various intervals. Over time, a strong $CHCl_3$ absorption appeared. Further, there was a consistent

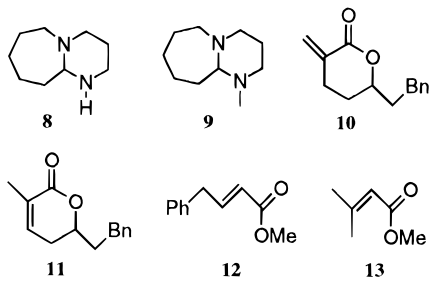


Figure 1. Structures of materials **8**−**13**.

reduction in the intensity of the C6-methylene absorption (60 MHz, δ 2.35, bs). The intensity was reduced to half after 12 d at 30−35 °C. Some decomposition (not investigated) commenced thereafter. That the reduction in C6-methylene absorption intensity was necessarily due to deuterium incorporation was supported further from EIMS of such a DBU: the M^+ signal increased from m/z 152 to 153 (100%). Though the above decomposition is not understood, only one deuterium atom incorporation bears significance. Stereoelectronic considerations suggest that only the C6-methylene hydrogen, which is orthogonal to the σ plane of the adjacent C=N double bond in the rigid bicyclic structure of DBU, must be exchanged. To determine whether this deuterium came exclusively from $CDCl_3$ and not from DCl, which may be present in samples of $CDCl_3$, and also whether the isomerization was indeed base catalyzed, two discrete experiments were performed: (a) mixing DCl-free $CDCl_3$ (filtered through basic Al_2O_3 of Brockmann grade I) and DBU showed repetition of the facility of deuterium incorporation and the remarkable rise in the $CHCl_3$ absorption and (b) a reaction of **6b** in THF with 1 equiv of DBU was as fast as the one in $CDCl_3$. Thus, while the first experiment confirmed $CDCl_3$ as the primary source of deuterium, the second experiment proved, beyond doubt, that all the isomerizations in the present study are only base-catalyzed. Both the experiments show little catalytic role of DCl. Otherwise, had all the deuterium come only from DCl and none from $CDCl_3$, the enhancement in $CHCl_3$ absorption must not have been observed.

The dienolate formed on H^+ abstraction by DBU from C5 of the 3,4-didehydrooxepanones may pick up D^+ from either $CDCl_3$ or $[DBU-D]^+$ to result in the observed C3-deuterated-4,5-didehydro- and the C5-deuterated-3,4-didehydro-2-oxepanones. These species will, of course, react again in an iterative process to generate the eventually observed C3,C5-dideuterated materials.

3. Significance of the Imine Double Bond. (i-Pr)$_2$NEt, Et_3N, and DABCO were also attempted, but they all failed to bring about the deconjugation in **6**. In each instance, the starting material was recovered quantitatively. The success of DBU at the above isomerizations clearly established its superiority over the other common nitrogeneous bases and invited a better understanding of the inherent reasons. To this end, DBU was reduced to the corresponding fully saturated species **8** (Figure 1) and allowed to react with **6b** in $CDCl_3$. ^1H NMR monitoring confirmed no isomerization even after 24 h. The alternate 1,4-addition of the amine[21] to the lactone did not take place either. Identical results were obtained from the related 8-methyl derivative **9**. These failures, when taken together with the success of DBU, point to a definite positive role of the imine double bond

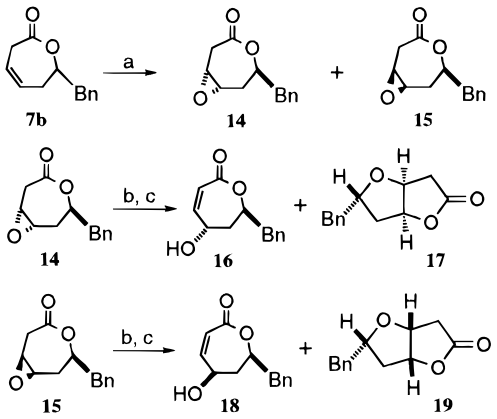
in DBU in the above deconjugations. The structural similarity between DBU and DBN allowed us to consider the latter as well. The material **6b** reacted smoothly with DBN, and 90% of **7b** was formed in 2.5 h. Though DBN appears slightly better than DBU, economy approves DBU. Clearly, the positive role of DBU must be ascribed to its enamine character.

4. Attempted Deconjugation of Systems Other than the 7-Ring Lactones: A Comparison. Enthused with the success of DBU-promoted deconjugations, we wished to study the smaller δ-valerolactones and acyclic examples. In the event, DBU was added to a $CHCl_3$ solution of a mixture of 3-methylidene-6-(2-phenethyl)-δ-valerolactone (**10**) and 3-methyl-3,4-didehydro-6-(2-phenethyl)-δ-valerolactone (**11**) to notice a very clean transformation of the former into the latter. The *exo*-methylene hydrogens in **10** [δ 6.5 (q, $J = 2$ Hz) and δ 5.6 (q, $J = 2$ Hz)] disappeared and the signal for the olefinic hydrogen in **11** [δ 6.6 (1H, m)] intensified. Further deconjugation in **11** did not occur. To the best of our information, this appears to be the first report on such an isomerization. The facility with which this isomerization took place is indeed remarkable, although in the cycloalkanone series similar isomerizations have been reported with the use of $RhCl_3 \cdot 3H_2O$ in a mixture of $CHCl_3$ and EtOH under conditions of reflux[22] and with *t*-BuOK in *t*-BuOH at 50−55 °C,[23] both for several hours. Deprotonation of **10** at C4 by DBU followed by protonation of the resultant allyl anion must constitute the necessary pathway for the observed isomerization.

Acyclic α,β-unsaturated esters were found to be inert to DBU. The *trans*-methyl 3-benzylacrylate (**12**) did not react even though the hydrogens on the γ-position are considered more reactive than the C5-hydrogens in the 3,4-didehydro-2-oxepanones for their enhanced acidity due to (a) the additional benzylic nature and (b) the *transoid* disposition to the ester function. Ethyl 3,3-dimethylacrylate (**13**), which has a *cisoid* γ-methyl resembling the C5-methylenes in the 3,4-didehydro-2-oxepanones, was also inert to DBU.

The inertness of **12** and **13** to deconjugative isomerization led us to study a 4-substituted oxepanone to ascertain the site of isomerization (*endo*- vs *exo*-cyclic). Our choice of substrate was **6e**, which was readily prepared from menthone in an overall 50% yield. In the event, **6e** was mixed with 1 equiv of DBU in $CDCl_3$, and a very slow reaction was noted. The only product **7e** (clearly observable from ^{1}H NMR only after 30 h) arose from endocyclic deconjugation. The diminution in the characteristic olefinic ^{1}H absorption at δ 5.86 (t, $J = 1.2$ Hz) in **6e** led to a new absorption at δ 5.44 (br s). This much slower rate of deconjugation in comparison to the other 7-ring species is due presumably to the steric effects arising from both of the ring substituents. Two interesting points, therefore, emerge: (a) the *cisoid* γ-methylene is appreciably more susceptible to H^+ abstraction by DBU than the *transoid* γ-methyl in α,β-unsaturated 2-oxepanones, and (b) while the *cisoid* γ-methylene in α,β-unsaturated-2-oxepanones is reactive, the *cisoid* γ-methyl in the acyclic unsaturated esters is not. In the rigid conformation of **6**, all but one (C6) ring atoms are nearly coplanar for the requirement of delocalization.[24] This causes considerable strain in the molecule and also fixes one of the two C5-hydrogens orthogonal to the olefin's σ plane for their effective interaction. These two are believed to contribute to the observed lability of the 2-oxepanones to DBU. While the orthogonality factor will raise the acidity of the hydrogen considerably, the relief from ring strain on deconjugation may be equally significant.

Scheme 2. Transformation of 7b into Bicyclic Species 17 and 19



[a] Reagents: (a) peracid, $CHCl_3$, rt; (b) K_2CO_3, DMF; (c) 5% aqueous HCl. The materials **14**−**19** are mixtures of diastereomers. For reasons of clarity, only one diastereomer of each is shown.

5. Application to the Synthesis of a Pharmacophore. The above deconjugation in the 2-oxepanones is important to synthetic chemists. The favorable economy, the operational simplicity, and the possible further synthetic transformations of the deconjugated materials are noteworthy and worth exploitation in fruitful synthetic endeavors. In demonstration of such an utility, **7b** was reacted with *m*-CPBA. From the mixture of the two oxiranes produced, the less polar material was the *trans*-**14** and the more polar the *cis*-**15** (**Scheme 2**; **14**:**15** = 2.7:1.0). The *cis*/*trans* assignments of the oxiranes were made from the X-ray structure of a bicyclic derivative (**23**) of the *cis*-oxirane (vide infra).

The *trans*-**14** was reacted further as shown to afford a mixture of *trans*-7-benzyl-3,4-didehydro-5-hydroxy-2-oxepanone (**16**) and 7-*exo*-benzyl-2,6-dioxa-3-oxobicyclo-[3.3.0]octane (**17**). The ratio **16**:**17** in the mixture was found to be dependent on the duration of the reaction; a longer reaction time favored the bicyclic species **17**. The *cis*-**15**, on the contrary, furnished predominantly the bicyclic material **19** under identical conditions. The related *cis*-7-benzyl-3,4-didehydro-5-hydroxy-2-oxepanone (**18**) was formed, if at all, in small amounts only (TLC) and escaped isolation. That the materials **17** and **19** were epimeric was evident from very similar ^{1}H absorptions. While a 2D ^{1}H spectrum helped to locate the various hydrogens in **17**, a ROESY spectrum established the cis relationship of the benzyl group and the hydrogens on the ring junctions. There were interactions observed between the Ph group and the hydrogen on C5 and between the benzylic methylene and the hydrogen on C8,

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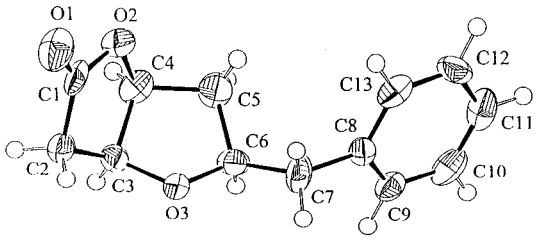
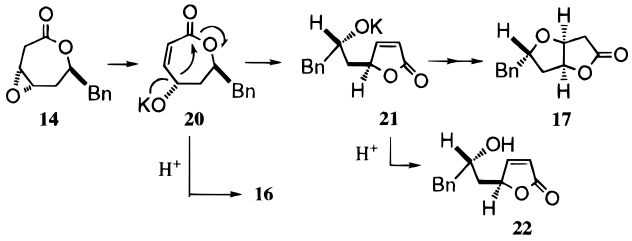


Figure 2. ORTEP plot of the X-ray crystal structure of **19**. Selected bond lengths (Å) bond angles (deg), and torsion angles (deg): O2−C4 1.459(7), C1−O2 1.365(7), C1−O1 1.193(7), C3−O3 1.424(7), C6−O3 1.444(7), O1−C1−O2 120.3(6), C1−O2−C4 111.1(5), C3−O3−C6 107.5(5), O2−C4−C5 110.3(6), C7−C6−C5−C4 141.2(6), C3−O3−C6−C7 162.5(5), C8−C7−C6−C5 62.2(8), C9−C8−C7−C6 76.9(9).

Scheme 3. Plausible Pathway for the Transformation of 14 into 17



which is cis to the hydrogen on the adjacent ring junction. The stereostructures of its progenitor, the oxirane **14**, must, therefore, be treated as confirmed. Obviously, the stereostructure of the other oxirane must be as in **15** and that of the bicyclic species derived from it as **19**. This was confirmed further from a single-crystal X-ray structure determination of **19**. An ORTEP plot along with some characteristic structural data on **19** are presented in Figure 2.

A plausible pathway for the transformation of **14** into **17** is given in Scheme 3. The intermediacy of the γ-lactone **22**, produced from the unreacted **21** on acidification, was confirmed from its isolation and spectral characterization. The significant spectral features are the ^{1}H absorptions at δ 7.57 (1H, dd, J = 5, 1.5 Hz) and δ 6.10 (1H, dd, J = 5, 2 Hz) for the olefinic hydrogens and at δ 5.25 (1H, td, J = 6.5, 1.5 Hz) for the hydrogen at C5. The IR absorption at 1740 cm^{-1} for the carbonyl supports the assignment. Likewise, the unreacted **20** will produce, on acidification, the observed **16**. A similar sequence may be considered for the conversion of **15** into **19**.

The bicyclo[3.3.0] unit present in **17** and **19** is notably present in plumeria and allamanda iridoids such as plumericin (**23**) (Figure 3), allamcin (**24**), and allamandin (**25**), which exhibit cytotoxic, antileukemic, antimicrobial, and antifungal properties,[25] in goniofufurone (**26**), which is an antitumor styryllactone,[26] in delesserine (**27**) and dilaspirolactone (**28**), which exhibit anticoagulant properties,[27] and in piptosidin (**29**).[28] This bicyclic skeleton, which may also serve as an useful synthon in organic

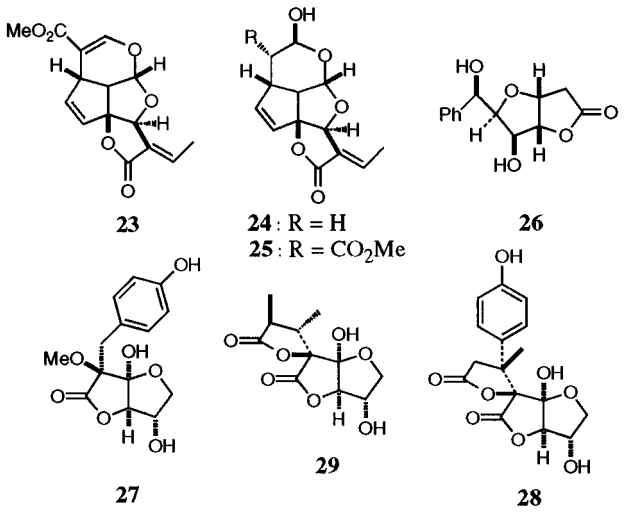


Figure 3. Structure of the naturally occurring materials **23**−**29**.

syntheses,[29] has recently been the focus of attention of several chemists.[30]

Conclusion

In conclusion, we have demonstrated DBU as a base of choice for the deconjugation of 3,4-didehydro-2-oxepanones. Other nitrogeneous bases such as (i-Pr)$_2$NEt, Et$_3$N, and DABCO failed. LDA and KH, which are much stronger than DBU, also failed. The reactions are base-promoted and cause deuterium incorporation at positions 3 and 5 of 2-oxepanones and position 6 of DBU when conducted in $CDCl_3$. The deconjugated species are useful for further synthetic manipulations. This is demonstrated by preparing a key pharmacophore unit present in a class of natural products of medicinal significance. Unlike the nonregiospecific photodeconjugation of 2-cyclooctenones, the present isomerizations are only endocyclic in nature and, hence, regiospecific. The onset of equilibration in the 7-benzyl derivatives is indeed noteworthy and must provoke investigations so as to understand the reason(s) for the same.

Experimental Section

Melting points were determined on an electrothermal apparatus in open capillary tubes and are uncorrected. ^{13}C NMR spectra were measured on Bruker DRX-300 at 75 MHz. Elemental analyses were performed on a Perkin-Elmer 240C instrument. Samples were dried in a vacuum desiccator over anhyd $CaCl_2$ before the elemental analysis. The other general remarks are as reported elsewhere.[17]

2-Benzyl-2-carbomethoxycyclohexanone (**2b**). This material was prepared using KF−Al_2O_3 as a base.[31] In the event, KF−Al_2O_3 (4.80 g, 30.0 mmol of KF) was added to a solution of 2-carbomethoxycyclohexanone (1.56 g, 10.0 mmol) and $PhCH_2Br$ (2.10 g, 12.0 mmol) in dry CH_3CN (30 mL). The mixture was stirred at rt for 5 h. Filtration and purification

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furnished the pure product; 2.26 g, 92%; ^{1}H NMR (60 MHz) δ 7.0 (5H, s), 3.5 (3H, s), 3.2 (1H, d, J = 14 Hz), 2.7 (1H, d, J = 14 Hz), 2.5−2.0 (m, 2H), 2.0−1.2 (m, 4H); IR (film) 1720, 1700 cm^{-1}.

2-Benzylcyclohexanone (3b). A solution of **2b** (1.132 g, 4.6 mmol) in anhyd DMF (18.5 mL) was mixed with anhyd LiCl (0.39 g, 9.2 mmol) and heated to 145−150 °C under N_2 for 7 h. The mixture was cooled to rt, poured into cold 5% aqueous $NaHCO_3$ (75 mL), extracted with ether (3 × 30 mL). The combined extracts were washed with brine (1 × 25 mL), dried, filtered, and concentrated. A chromatographic purification furnished **3b** (0.778 g, 90%) as an oil. This material exhibited the previously reported ^{1}H and IR spectral characteristics.[13,32]

For the above decarboxylation with LiCl in DMF, we have discovered that 4 mL of DMF for every mmol of the substrate constituted the optimum. With lower volumes of DMF, considerably large amounts of the corresponding carboxylic acids were formed.[33]

7-Benzyl-2-oxepanone (4b). To an ice-cold solution of **3b** (0.376 g, 2.0 mmol) in $CHCl_3$ (10 mL) was added *m*-CPBA (70%, 0.740 g, 4.0 mmol). The mixture was allowed to come to rt and stirred for 50 h. This was poured into 20% aqueous Na_2SO_3 (10 mL), stirred for 30 min, and diluted with $CHCl_3$ (10 mL). The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (2 × 5 mL). The combined extracts were washed with 10% aqueous $NaHCO_3$ (2 × 10 mL) and brine (1 × 10 mL), in that order. The organic solution was dried, filtered, and concentrated to furnish a residue that was chromatographed to afford **4b**: 0.40 g, 98%; ^{1}H NMR (60 MHz) δ 7.15 (5H, s), 4.6−4.0 (1H, m), 3.0−2.3 (4H, m), 2.0−1.1 (6H, m); IR (film) 1720 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.58; H, 7.71.

***trans*- and *cis*-7-Benzyl-3-(selenophenyl)-2-oxepanones (5b).** *n*-BuLi (1.6 M, 0.75 mL, 1.2 mmol) was added to a solution of (*i*-Pr)$_2$NH (0.122 g, 1.2 mmol) in THF (1.5 mL) at −80 °C. This was stirred for 15 min and a solution of **4b** (0.204 g, 1.0 mmol) in THF (2 mL) added dropwise. After 20 min, a THF solution of PhSeBr (1.0 mL, 1.2 mmol) [a solution of PhSeBr in THF was prepared by mixing, for 10 s, a solution of Br_2 (96 mg, 0.6 mmol) in THF (0.5 mL) with a solution of diphenyl diselenide (188 mg, 0.6 mmol) in THF (0.5 mL)] was added, all in one portion. The reaction was allowed to come to rt and worked up. The mixture was diluted with Et_2O (10 mL) and acidified with 5% aqueous HCl (5 mL). The layers were separated, and the organic layer was washed successively with H_2O (2 × 5 mL) and 10% aqueous $NaHCO_3$. The organic solution was dried, filtered, and concentrated to furnish a residue that was purified for **5b** by chromatography; 0.274 g, 76%. Both the *cis*-**5b** and *trans*-**5b** were isolated and characterized separately. *Trans*-**5b**: ^{1}H NMR (400 MHz) δ 7.55−7.20 (10H, m), 5.25 (1H, m), 4.25 (1H, t, J = 4 Hz), 3.10 (1H, dd, J = 12, 6 Hz), 2.85 (1H, dd, J = 14, 6 Hz), 2.10 (2H, m), 2.00 (1H, td, J = 12, 3 Hz), 1.90−1.75 (2H, m), 1.65−1.55 (1H, m); IR 1710, 1600 cm^{-1}. *cis*-**5b**: ^{1}H NMR (400 MHz) δ 7.60−7.20 (10H, m), 4.50 (1H, m), 4.20 (1H, dd, J = 12, 2 Hz), 3.1 (1H, dd, J = 12, 6 Hz), 2.82 (1H, dd, J = 12, 6 Hz), 2.12 (1H, bd, J = 14 Hz), 2.00−1.82 (3H, m), 1.65−1.55 (1H, m), 1.48−1.35 (1H, m); IR 1710, 1600 cm^{-1}.

7-Benzyl-3,4-didehydro-2-oxepanone (6b). H_2O_2 (350 μL of a 30% aqueous solution mixed with 700 μL of H_2O, 3.0 mmol) was added dropwise to a solution of **5b** (0.359 g, 1.0 mmol) and pyridine (0.158 g, 2.0 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The solution was stirred for 20 min at 0 °C and at rt for 20 min. This was poured into a mixture of CH_2Cl_2 (10 mL) and 5% aqueous $NaHCO_3$ (10 mL) and stirred for 5 min. The layers were separated, and the aqueous solution was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic extracts were washed successively with cold 5% aqueous HCl (1 × 10 mL), H_2O (1 × 10 mL), and brine (1 × 10 mL). Drying and solvent removal furnished a residue that was chromatographed to give **6b**: 0.162 g, 80%; ^{1}H NMR (300 MHz) δ 7.34 (5H, m), 6.41−6.34 (1H, td, J = 12, 4.5 Hz), 5.99−5.95 (1H, td, J = 12, 1.8 Hz), 4.57−4.49 (1H, dq, J = 7.5, 1.8 Hz), 3.19−3.12 (1H, dd, J = 14, 6.5 Hz), 2.91−2.84 (1H, dd, J = 14, 7.0 Hz), 2.54−2.26 (2H, m), 2.15−1.90 (2H, m); IR (film) 1700, 1630 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.93. Found: C, 77.33; H, 7.05.

3,4-Dehydro-7-(*p*-methoxybenzyl)-2-oxepanone (6c). The above protocol for the transformation of **2b** into **6b** was adopted. The material **3c**, which has previously been prepared by allowing *N*-(1-cyclohexenyl)pyrrolidine to combine with 4-methoxybenzyl chloride,[11] was prepared in 88% yield from **2c**, and **2c** itself was prepared from 2-carbomethoxycyclohexanone in 90% yield. The yields of the other purified intermediates and **6c** itself and their spectral characteristics are as follows:

2-Carbomethoxy-2-(*p*-methoxybenzyl)cyclohexanone (2c): 90%; ^{1}H NMR (60 MHz) δ 7.1−6.8 (4H, m), 3.8 (3H, s), 3.7 (3H, s), 3.3−2.7 (2H, 2d, J = 14 Hz), 2.6−2.2 (4H, m), 2.0−1.4 (4H, m).

7-(*p*-Methoxybenzyl)-2-oxepanone (4c): 95%; ^{1}H NMR (60 MHz) δ 7.2−6.6 (4H, m), 4.5−3.9 (1H, m), 3.7 (3H, s), 3.1−2.4 (2H, 2 dd, J = 13, 5 Hz), 2.6−2.3 (2H, m), 2.1−1.1 (6H, m); IR (film) 1710, 1600 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71. 58; H, 7.90.

***trans*- and *cis*-7-(*p*-Methoxybenzyl)-3-(phenylselenenyl)-2-oxepanone (5c).** This was a 2:1 mixture of the expected *trans*- (δ 5.13, C7-H) and *cis*-isomers (δ 4.40, C7-H) (75% yields), respectively. The chromatographic separation was difficult because of the very little difference in the polarities (TLC). However, a small sample of *trans*- **5c** was obtained in a state of purity. *trans*- **5c**: ^{1}H NMR (300 MHz) δ 7.55−6.80 (4H, m), 5.13 (1H, m), 4.19 (1H, m), 3.78 (3H, s), 3.03−2.97 (1H, dd, J = 15, 6 Hz), 2.81−2.74 (1H, dd, J = 15, 6 Hz), 2.12−2.05 (2H, m), 2.05−1.50 (4H, m); IR (film) 1705, 1600 cm^{-1}.

7-(*p*-Methoxybenzyl)-3,4-didehydro-2-oxepanone (6c): 82%; ^{1}H NMR (300 MHz) δ 7.16 (2H, d, J = 9 Hz), 6.84 (2H, d, J = 9 Hz), 6.41−6.33 (1H, td, J = 12, 4.5 Hz), 6.00−5.94 (1H, td, J = 12, 1.8 Hz), 4.51−4.43 (1H, m), 3.79 (3H, s), 3.12−3.05 (1H, dd, J = 14, 6 Hz), 2.85−2.78 (1H, dd, J = 14, 6 Hz), 2.60−2.25 (2H, m), 2.07−1.90 (2H, m); IR (film) 1695, 1600 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.24; H, 7.20.

2-Carbomethoxy-2-(2-phenethyl)cyclohexanone (2d). 2-Carbomethoxycyclohexanone (0.78 g, 5 mmol) was added dropwise to an oil-free suspension of NaH (0.24 g of a 60% oil dispersion, 6.0 mmol) in dry DMF (5 mL) and C_6H_6 (15 mL) and the resulting mixture stirred until the gas evolution ceased (10 min). NaI (75 mg, 0.5 mmol) and 2-phenethyl bromide (0.93 g, 5 mmol) were added and the contents refluxed for 1 h. The reaction mixture was cooled to rt, mixed with saturated aqueous NH_4Cl (20 mL), and extracted with ether (2 × 15 mL). The organic extracts were washed with H_2O (2 × 15 mL) and brine (1 × 15 mL), dried, and concentrated. The crude material was purified by chromatography to furnish the desired **2d**: 0.94 g, 72%; ^{1}H NMR (60 MHz) δ 7.1 (5H, s), 3.7 (3H, s), 3.0−1.2 (12H, m). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.68; H, 7.86.

3,4-Didehydro-7-(2-phenethyl)-2-oxepanone (6d). This material was prepared from **2d** by following the reaction sequence and the experimental procedures given above for the transformation of **2b** into **6b**. The synthesis of **3d** has previously been accomplished in 15% yield by allowing palladium-assisted coupling of styrene with the Li-enolate of cyclohexanone.[15] The yields of **4d**, **5d**, and **6d** and their spectral characteristics are as follows:

7-(2-Phenethyl)-2-oxepanone (4d): 75%; ^{1}H NMR (300 MHz) δ 7.32−7.17 (5H, m), 4.21−4.16 (1H, m), 2.88−2.50 (4H, m), 2.12−1.4 (8H, m); IR (film) 1710 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2$ C, 77.03; H, 8.31. Found: C, 77.23; H 8.50.

***trans*- and *cis*-7-(2-phenethyl)-3-(phenylselenenyl)-2-oxepanone (5d):** 82%; ^{1}H NMR (60 MHz) δ 5.4−4.9 and 4.9−4.5 (1H, m), 4.3−3.8 (1H, m), 3.0−2.6 (2H, m); IR (film) 1700 cm^{-1}.

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3,4-Didehydro-7-(2-phenethyl)-2-oxepanone (6d): 80%; ^{1}H NMR (300 MHz) δ 7.32−7.17 (5H, m), 6.42−6.35 (1H, td, J = 12, 4.5 Hz), 6.02−5.96 (1H, td, J = 12, 2 Hz), 4.32−4.24 (1H, m), 2.86−2.72 (2H, m), 2.58−2.32 (2H, m), 2.17−2.1.95 (3H, m), 1.90−1.80 (1H, m); IR (film) 1685 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.45. Found: C, 77.87; H 7.60.

3,4-Didehydro-7-methyl-2-oxepanone (6a). This material was synthesized from 2-methylcyclohexanone by following the above protocol for the transformation of **3b** into **6b**. The material **4a**[16] was obtained from **3a** in 80% yield. The yield and the spectral characteristics of the intermediate **5a** are given below. The species **5a** was transformed into the known **6a**[16] in 76% yield.

3-(Phenylselenenyl)-7-methyl-2-oxepanone (5a): 70% (isomeric mixture); ^{1}H NMR (60 MHz) δ 7.7−7.2 (5H, m), 5.2−4.7 (1H, m), 4.3−4.0 (1H, bt), 1.3 (3H, d, J = 6 Hz); IR (film) 1705 cm^{-1}.

3,4-Didehydro-7-isopropyl-4-methyl-2-oxepanone (6e). Like the synthesis of **6a** from **3a**, the synthesis of **6e** commenced from menthone (**3e**). The oxidation of **3e** proceeded in 70% yield to generate the known **4e**.[16] The yields and the spectral characteristic of **5e** and **6e** are given below:

***cis*- and *trans*-3-(phenylselenenyl)-7-isopropyl-4-methyl-2-oxepanone (5e):** 60%; ^{1}H NMR (60 MHz) δ 7.6 (2H, bs), 7.3 (3H, bs), 4.6 (1H, bs), 4.3−4.0 (1H, m), 1.2 (3H, d, J = 6.5 Hz), 1.0 (6H, 2d, J = 6.5 Hz).

3,4-Didehydro-7-isopropyl-4-methyl-2-oxepanone (6e): 60%; ^{1}H NMR (300 MHz) δ 5.86 (1H, t, J = 1.2 Hz), 4.06−4.01 (1H, ddd, J = 2.7 Hz), 2.54−2.44 (1H, td, J = 18, 6 Hz), 2.33−2.22 (1H, m), 1.94 (3H, s), 1.00−0.97 (6H, 2d, J = 6.6 Hz). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.38; H, 9.59. Found: C, 71.59; H, 9.85.

General Procedure for Isomerization. The lactones **6a**−**e** (0.05 mmol) and DBU (0.076 g, 0.05 mmol) were mixed together in $CHCl_3$ (2 mL) [or $CDCl_3$ (0.4 mL) if the reaction was to be monitored by ^{1}H NMR] and kept aside [for 3 h for **6a-d** (but for the equilibration studies when the reactions were monitored for as long as 60 h) and for 30 h for **6e**] while the progress was monitored by TLC. The workup involved dilution with Et_2O (10 mL) and washing with cold 2% aqueous HCl (2 × 5 mL), water (1 × 5 mL), and brine (1 × 5 mL). The organic solution was dried, concentrated to furnish a residue, and purified. The material balance was nearly quantitative.

7-Benzyl-4,5-didehydro-2-oxepanone (7b): ^{1}H NMR (300 MHz) δ 7.34−7.22 (5H, m), 5.69−5.61 (1H, m), 5.58−5.48 (1H, m), 4.93−4.85 (1H, m), 3.67−3.60 (1H, md), 3.13−3.06 (1H, dd, J = 14, 6.8 Hz), 3.07−2.99 (1H, dd, J = 16.5, 8.7 Hz), 2.88−2.81 (1H, dd, J = 14, 6 Hz), 2.45−2.41 (2H, m); IR (film) 1720, 1650 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.93. Found: C, 77.30; H, 7.10.

7-(*p*-Methoxybenzyl)-4,5-didehydro-2-oxepanone (7c): ^{1}H NMR (300 MHz) δ 7.17 (2H, d, J = 8.5 Hz), 6.85 (2H, d, J = 8.5 Hz), 5.69−5.62 (1H, td, J = 11, 3.6 Hz), 5.52 (1H, m), 4.88−4.79 (1H, q, J = 6 Hz), 3.79 (3H, s), 3.07−3.00 (1H, dd, J = 14, 6.6 Hz), 2.82−2.75 (1H, dd, J = 14, 6.3 Hz), 2.42−2.40 (2H, m). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.20; H 7.18.

7-(2-Phenethyl)-4,5-didehydro-2-oxepanone (7d): ^{1}H NMR (300 MHz) δ 7.29−7.14 (5H, m), 5.66−5.47 (2H, m), 4.61−4.54 (1H, m), 2.86−2.69 (2H, m), 2.51−2.41 (1H, m), 2.32−2.26 (1H, d, J = 18 Hz), 2.07−2.00 (1H, m), 1.86−1.77 (1H, m); IR (film) 1715 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.45. Found: C, 77.94; H, 7.65.

4,5-Dehydro-7-isopropyl-4-methyl-2-oxepanone (7e): ^{1}H NMR (300 MHz) δ 5.44 (1H, bs), 4.46−4.39 (1H, ddd, J = 2.7 Hz), 3.80 (1H, bd, J = 16 Hz), 2.86 (1H, d, J = 16 Hz), 2.44−2.23 (2H, m), 1.93−1.82 (1H, m), 1.79 (3H, s), 1.00−0.96 (6H, 2d, J = 6.6 Hz). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.38; H, 9.59. Found: C, 71.53; H, 9.83.

1,8-Diazabicyclo[5.4.0]undecane (8). Glacial AcOH (0.395 g, 6.5 mmol) was added to an ice-cold solution of DBU (1.0 g, 6.5 mmol) in EtOH (20 mL). To the stirred solution was then added $NaBH_4$ (0.25 g, 6.5 mmol) in small portions. The reaction was stirred at rt for 2 h whereupon some white solid separated out. The EtOH was removed and the residue taken with EtOAc (20 mL) and H_2O (2 mL). This resulted in a clear biphasic solution to which was added enough anhyd Na_2SO_4 to absorb the water. Filtration and solvent removal furnished **8**: 0.80 g, 80%. Absence of the broad multiplet at δ 2.0 for the allylic CH_2 in DBU indicated a complete reduction: ^{1}H NMR (60 MHz) δ 3.8−2.9 (1H, br m), 2.9−2.3 (7H, m), 1.9−1.2 (10H, br m). Anal. Calcd for $C_9H_{18}N_2$: C, 70.08; H, 11.76; N, 18.16. Found: C, 69.76; H, 12.00; N, 18.48.

8-Methyl-1,8-diazabicyclo[5.4.0]undecane (9). MeI (2.0 g, 14 mmol) was added to a stirring solution of DBU (1.52 g, 10 mmol) in dry benzene (25 mL) at rt. A white precipitate separated out immediately. The stirring was continued for 30 min, and then the solvent was evaporated. The white solid thus received was taken in EtOH (20 mL) and treated with, in portions and under stirring, $NaBH_4$ (0.38 g, 10 mmol). After 2 h, the EtOH was evaporated and the residue was dissolved in EtOAc (20 mL) and H_2O (3 mL). Enough Na_2SO_4 was added to absorb H_2O. Filtration and solvent removal furnished **9**: 1.52 g, 90%; ^{1}H NMR (300 MHz) δ 2.85−2.54 (7H, m), 2.47 (3H, s), 1.80−1.59 (10H, m). Anal. Calcd for $C_{10}H_{20}N_2$: C, 71.38; H, 11.98; N, 16.64. Found: C, 71.15; H, 12.24; N, 16.88.

***trans*- and *cis*-7-Benzyl-4,5-epoxy-2-oxepanones (14 and 15).** To a stirred solution of **7b** (44 mg, 0.22 mmol) in $CHCl_3$ (0.4 mL) at 5 °C was added $PhCO_3H$ (0.56 mL of a 0.5 M solution in $CHCl_3$). The mixture allowed to come to rt and stirred for 15 h. Saturated aqueous Na_2SO_3 (3 mL) was added, and the contents were stirred for 30 min. The reaction was partitioned between $CHCl_3$ (15 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (2 × 5 mL). The combined organic extracts were washed with 10% aqueous $NaHCO_3$ (2 × 7 mL) and brine (7 mL). Drying, removal of solvent, and chromatography furnished **14** (28 mg, 60%, mp 78−79 °C) and **15** (14 mg, 30%, mp 86−87 °C), both as powdery solids. **14**: ^{1}H NMR (400 MHz) δ 7.35−7.15 (5H, m), 4.30 (1H, m), 3.30 (1H, m), 3.20−3.10 (2H, m), 3.05 (1H, dd, J = 12, 6 Hz), 2.96 (1H, dd, J = 15, 3 Hz), 2.85 (1H, dd, J = 12, 6 Hz), 2.45 (1H, d, J = 15 Hz), 2.16 (1H, ddd, J = 15, 10, 2 Hz); IR (KBr) 1720, 1590 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.61; H, 6.37. **15**: ^{1}H NMR (400 MHz) δ 7.35−7.20 (5H, m), 4.66 (1H, m), 3.41 (1H, unsym d, J = 15 Hz), 3.30 (1H, dd, J = 15, 6 Hz), 3.2 (2H, m), 3.05 (1H, dd, J = 15, 6 Hz), 2.78 (1H, dd, J = 15, 6 Hz), 2.37 (1H, dd, J = 18, 12 Hz), 2.18 (1H, ddd, J = 15, 4, 2 Hz); IR (KBr) 1730, 1590 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.64; H, 6.58.

***trans*-3,4-Didehydro-5-hydroxy-7-benzyl-2-oxepanone (16) and 7-*exo*-Benzyl-2,6-dioxa-3-oxobicyclo[3.3.0]-octane (17).** K_2CO_3 (90 mg, 0.66 mmol) was added to a solution of **14** (48 mg, 0.22 mmol) in DMF (1.0 mL). The mixture was stirred at rt for 2 h, and then 5 mL H_2O was added. This was extracted thoroughly with EtOAc (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried, and concentrated. The residue was chromatographed to afford **16** (36 mg, 75%) and **17** (10 mg, 20%). **16**: ^{1}H NMR (60 MHz) δ 7.2 (5H, s), 6.3 (1H, dd, J = 12, 3 Hz), 5.7 (1H, dd, J = 12, 1 Hz), 4.9−4.2 (2H, m), 2.9 (2H, dd, J = 14, 6 Hz), 2.3−1.9 (2H, m); IR (film) 3420, 1695, 1625, 1490 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.41; H, 6.29. **17**: ^{1}H NMR (300 MHz) δ 7.33−7.18 (5H, m), 5.09−5.06 (1H, t, J = 5 Hz), 4.82−4.79 (1H, t, J = 5 Hz), 4.40−4.31 (1H, sextet, J = 6 Hz), 2.95 (1H, dd, J = 12, 6 Hz), 2.85 (1H, dd, J = 12, 6 Hz), 2.75 (1H, dd, J = 18, 6 Hz), 2.65 (1H, d, J = 18 Hz), 2.35−2.29 (1H, dd, J = 12, 4 Hz), 1.80−1.71 (1H, ddd, J = 12, 9, 4 Hz); ^{13}C NMR δ 175.7, 137.3, 129.1, 128.3, 126.4, 84.5, 78.6, 77.6, 40.5, 38.1, 36.4; IR (film) 1770, 1590 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.48; H, 6.60.

7-*endo*-Benzyl-2,6-dioxa-3-oxobicyclo[3.3.0]octane (19). This material was prepared from the *cis*-oxirane **15** (48 mg, 0.22 mmol) by treatment with K_2CO_3 (90 mg, 0.66 mmol) in dry DMF for 2 h. Usual workup as above for the transformation of **14** into **16** and **17** and purification furnished **19**: 46 mg, 96%. This was recrystallized from a mixture of CCl_4 and petroleum ether: mp = 64 °C; ^{1}H NMR (300 MHz) δ 7.33−7.19 (5H, m), 5.04−4.99 (1H, m), 4.56−4.53 (1H, m), 4.26−

4.17 (1H, q, J = 7 Hz), 3.04−2.97 (1H, dd, J = 14, 7.2 Hz), 2.86−2.80 (1H, dd, J = 14, 6.3 Hz), 2.75 (2H, d, J = 4.5 Hz), 2.44−2.34 (1H, q, J = 7.2 Hz), 2.07−1.99 (1H, ddd, J = 14.4, 7.5, 2.1 Hz).

3,4-Didehydro-5-(2-hydroxy-3-phenylpropyl)-γ-butyrolactone (22). On one occasion only, we were able to isolate a small amount of **22** from the reaction of **14** with K_2CO_3 in DMF (vide supra): ^{1}H NMR (80 MHz) δ 7.64−7.50 (1H, dd, J = 5 and 1.5 Hz), 7.50−7.10 (5H, m), 6.15−6.05 (1H, dd, J = 5, 2 Hz), 5.40−5.17 (1H, td, J = 6.5, 1.5 Hz), 4.28−3.90 (1H, m), 2.95−2.71 (2H, m), 2.14−1.8 (3H, t, J = 5 Hz); IR (film) 3340, 1740, 1590 cm^{-1}; EIMS m/z = 218 (M^+). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.61; H, 6.36.

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Supporting Information Available: Copies of ^{1}H NMR spectra of compounds **4b**−**e**, **6b**−**e** (all but **6b** without any deuterium; **6b** was obtained from a full equilibration experiment in $CDCl_3$ and, hence, possesses deuterium at positions 3 and 5), **7b**−**e** (**7b** was obtained from a full equilibration experiment in $CDCl_3$ and, hence, contains deuterium at positions 3 and 5), **14**, **15**, **17**, **19**, and **22**, ROESY and COSY of **17**, ^{13}C spectra of deuterated **6b** and **7b** (obtained from equilibrium experiments) and **17**, mass spectra of deuterated **7c** (from equilibration experiment) and deuterated DBU, and X-ray data for **19** (50 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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