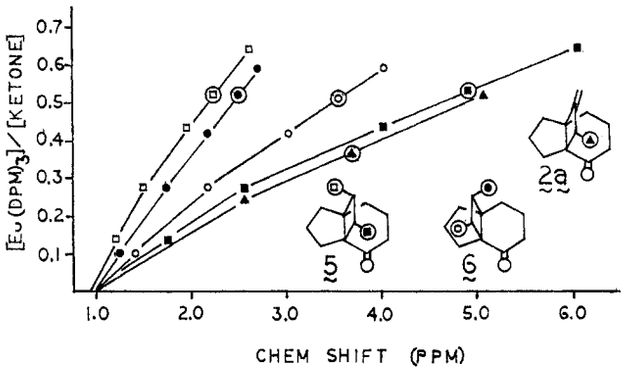

Figure 1.—Effect of nmr shift reagent on methyl groups at varying distances from binding site.

Experimental Section

10-Methyl-11-methylenetricyclo[4.3.2.0]undecan-2-one (2a).—A solution of 2.10 g (11.0 mmol) of 10,11-dimethyltricyclo-[4.3.2.0]undec-10-en-2-one (1)[7] in hexane (450 ml) was irradiated (Corex filter) for 5 hr. Progress of the reaction was monitored by the disappearance of 1 with glpc (3% DEGS, 8 ft × 0.125 in., 110°, 30 cc/min of He). The solvent was removed by distillation and the residue was short path distilled (68°, 0.20 mm) to afford 0.579 g of a four-component mixture. The major product **2a** (*ca.* 70% of mixture) was collected from glpc (20% Carbowax 1000M, 5.5 ft × 0.25 in., 150°, 85 cc/min of He): uv max (95% EtOH) 295 nm (ε 62); ir (CCl_4) 1690 cm^{-1}; nmr (CCl_4) δ 4.88 (m, 2, exo methylene), 2.3–1.1 (m, 13, all ring protons), 0.99 (d, J = 7.2 Hz, 3, methyl); mass spectrum (70 eV) m/e 190 (molecular ion).

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.89; H, 9.63.

Infrared spectra (CCl_4) of the three minor components, each of which comprised *ca.* 10% of the isolated product mixture, were very similar to that of **2a**. An nmr spectrum of the crude reaction mixture indicated that **2a** was the major component before glpc analysis.[4c]

10-Methyltricyclo[4.3.2.0]undecane-2,11-dione (4a).—A 0.630-g (3.27 mmol) quantity of ketone **2** in methylene chloride (100 ml) was cooled (−78°) and ozone was passed through the solution until ozone was detected in the effluent gas. The reaction solution was concentrated, and the resulting yellow oil in formic acid (10 ml) and 30% hydrogen peroxide (5 ml) was heated at reflux for 30 min. Concentration of the reaction solution left 0.590 g (94%) of diketone **4a**: mp 108–109°; ir (CCl_4) 1770 (cyclobutanone C=O) and 1705 cm^{-1} (cyclohexanone C=O); nmr (CCl_4) δ 2.5–1.1 (m, 13, all protons except CH_3), 0.93 (d, J = 6 Hz, 3, CH_3).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.02; H, 8.46.

Attempted Base Cleavage of Diketone 4a.—A 0.590-g (3.07 mmol) quantity of **4a** and 10% Na_2CO_3 solution (200 ml) were heated at reflux for 2 hr. The cool reaction mixture was extracted with ether (2 × 40 ml) and the combined extracts were washed with saturated NaCl solution (20 ml), dried ($MgSO_4$), concentrated, and sublimed (80°, 0.2 mm) to yield 0.380 g (64%) of recovered **4a**. Acidification of the aqueous phase followed by work-up as above separated an additional 0.050 g (8%) of **4a**.

Irradiation of Tricyclo[4.3.2.0]undec-10-en-2-one.—A solution of 211 mg of tricyclo[4.3.2.0]undec-10-en-2-one[7] in 55 ml of methylene chloride was irradiated (Corex filter) for 30 min. The solvent was removed by distillation and the residual oil was purified by glpc (20% DEGS, 10 ft × 0.25 in., 200°, 50 ml/min He) to give 1,1,2,2-tetrachloroethane and 154 mg (72%) of tricyclo[4.3.2.0]undecan-2-one as the only volatile products: uv max (95% EtOH) 293 nm (ε 26); ir (CCl_4) 1700 cm^{-1}; the nmr spectrum (CCl_4) is a complex absorption centered at *ca.* δ 1.9. This ketone is identical with a sample prepared by catalytic hydrogenation.

The *p*-toluenesulfonylhydrazone was recrystallized from methanol–water, mp 140–140.5°.

Anal. Calcd for $C_{18}H_{24}N_2O_2S$: C, 65.04; H, 7.28; N, 8.43. Found: C, 65.08; H, 7.25; N, 8.53.

Registry No.—**1**, 22241-70-9; **2a**, 38229-64-0; **4a**, 38229-65-1; tricyclo[4.3.2.0]undec-10-en-2-one, 22241-68-5; tricyclo[4.3.2.0]undecan-2-one, 38229-67-3; tricyclo[4.3.2.0]undecan-2-one *p*-toluenesulfonylhydrazone, 38229-68-4.

(13) All boiling points and melting points are uncorrected. Microanalyses were performed by Bernhardt Microanalytisches Laboratorium, Elbach uber Engelskirchen, West Germany. Infrared spectra were recorded using a Perkin-Elmer Model 257 grating spectrophotometer. All nmr spectra were determined using tetramethylsilane as an internal standard, with a Varian A-60 nmr spectrometer. Ultraviolet spectra were recorded with a Perkin-Elmer Model 202 spectrophotometer. Analytical gas–liquid partition chromatograms were determined using a Varian Aerograph 1200 flame ionization chromatograph, and preparative glpc separations were conducted using a Varian Aerograph 90-P-3 chromatograph. Irradiations were carried out using a Hanovia high-pressure mercury arc (450 W), internal probe, type L, with the filter specified.

O-Alkyl Cleavage of Methyl Esters by 1,5-Diazabicyclo[5.4.0]undecene-5

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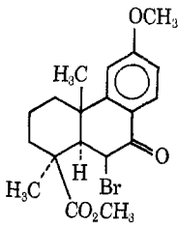
In connection with the synthesis of diterpenoid intermediates an improved yield of lactone **2** from bromo ketone **1** was required. The transformation of bromo ketone **1** to a mixture of lactone **2** (47% yield) and ester **3** (40% yield) by refluxing in collidine has been previously reported[2,3] along with the observation that treatment of bromo ketone **1** with sodium methoxide yields only elimination product **3**. The suggestion was offered that a major factor in the contrasting behavior of sodium methoxide and collidine might be the steric requirements of the bases for proton abstraction. Thus we initiated an investigation into the improvement of the yield of lactone **2** by utilizing a variety of bases that have greater steric requirements than collidine. As a result of this study, we now wish to report that the base 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) is useful for the *O*-alkyl cleavage of methyl esters.

Reaction of bromo ketone **1** with 2 equiv of DBU in 10 equiv of *o*-xylene at 165° for 5 hr gave product **5** in 92% yield in the form of a white, crystalline solid, mp 122.5–123.5°. The infrared spectrum showed absorptions at 1650 and 1600 cm^{-1} for the α,β-unsaturated ketone system. The nmr spectrum exhibited resonance signals for a doublet (J = 6 Hz) at δ 1.41 for the C-4 methyl group, a singlet at 1.73 for the C-10 tertiary methyl group, a singlet at 4.33 for the methoxy group, a doublet (J = 1.8 Hz) at 6.91 for the vinylic proton, a multiplet at 7.39 for the C-13 and C-14 protons, and a doublet (J = 9 Hz) at 8.98 for the C-11 proton. Neither lactone **2** nor elimination product **3** were found in the reaction mixture.

Additional evidence for structure **5** was the observation that elimination product **3** could be isolated in 90.5% yield if bromo ketone **1** was allowed to react for only 15 min. Since DBU is known to be a facile de-

(1) National Defense Education Act Graduate Fellow, 1971–1973.
(2) E. Wenkert, *et al.*, *J. Org. Chem.*, **30**, 713 (1965).
(3) E. Wenkert, *et al.*, *Can. J. Chem.*, **41**, 1924 (1963).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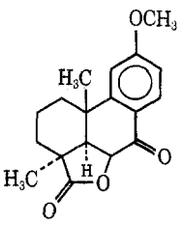
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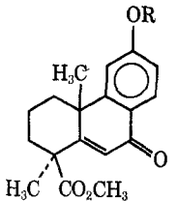
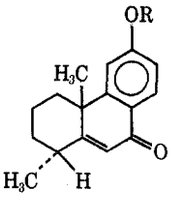
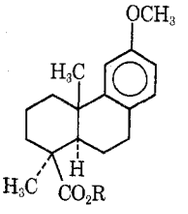

3, R = CH_3
4, R = H

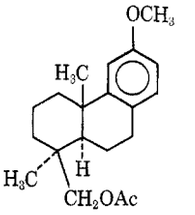

5, R = CH_3
6, R = H

hydrohalogenating agent,[4-8] the isolation of intermediate ester **3** indicates that **5** must have arisen from **1** by dehydrobromination and subsequent decarbomethoxylation. Support for the stereochemistry assigned to **5** is provided by the report[3] that **6** can be obtained from **4** in approximately 33% yield by dealkylation and subsequent decarboxylation with lithium iodide in refluxing collidine.[9,10]

Evidence that decarbomethoxylation of compounds **1** and **3** proceeded through *O*-methyl cleavage of the methyl ester and subsequent decarboxylation was provided by the following results. Treatment of ester **7** with 10 equiv of DBU in 10 equiv of *o*-xylene at a reaction temperature of 165° for 48 hr gave pure white crystalline acid **8** in 96.7% yield, mp 159–160° (lit.[11] mp 158–161°). When acetate **9** was treated with DBU in the same manner only starting material could be recovered from the reaction mixture. These results rule out the possibility that the conversion of ester **7** to acid **8** could have proceeded by the hydrolytic route. If this route had been operative acetate **9** would have been easily cleaved in comparison to ester **7**. Ester **7** (methyl *O*-methylpodocarpate) requires extremely severe conditions for ordinary hydrolysis.[12]

The generality of the cleavage reaction is demonstrated by the application of DBU to the cleavage of methyl *O*-methylpodocarpate (**7**) and the four esters described below.


7, R = CH_3
8, R = H


9

Methyl mesitoate is the classic example of a hindered ester. A solution of DBU (10 equiv) in 10 equiv of *o*-xylene was allowed to react at 165° for 48 hr to give a 94.6% yield of colorless crystals, mp 149–151° (lit.[13] mp 153–154°), which was identical by mixture melting point and ir with authentic mesitoic acid.

Methyl triisopropylacetate has also been utilized to confirm the ability of several reagents to cleave hindered esters.[11,14]

Triisopropylacetic acid was esterified with diazomethane, and the crude ester was treated with 10 equiv of DBU dissolved in 10 equiv of *o*-xylene at 165° for 48 hr to give a 91.2% yield of colorless crystals, mp 136–139°. One recrystallization from methanol–water gave material which was identical by mixture melting point and ir with an authentic specimen of triisopropylacetic acid.

In order to demonstrate that this reaction is not limited to hindered esters in very complex molecules, the simple ester, methyl palmitate, was treated with 10 equiv of DBU in 10 equiv of *o*-xylene at 165° for 48 hr. The resulting acid, mp 62–63°, was obtained in 93% yield and was identical by mixture melting point and ir with authentic palmitic acid.

Methyl 3β-acetoxy-Δ_5-etienate contains both a hydrolytically sensitive functionality and a relatively hindered ester group, and was used in the investigation of the lithium iodide/refluxing lutidine system as a selective ester cleavage reagent. With both iodide and DBU SN2 displacement of the acetate group is sterically hindered and attack at the acetate carbonyl is energetically unfavorable; therefore, reasonable selectivity can be achieved. After 8 hr reflux, the lithium iodide method gave 25–28% of starting material, 49–51% of the desired acetoxy acid, and 5–10% of the hydroxy acid resulting from hydrolytic loss of the acetate group.[10]

A solution of DBU (10 equiv) and the acetoxy ester in 10 equiv of *o*-xylene was allowed to react at 165° for 3.5 hr. The reaction time was optimized for maximum selectivity. Glc comparison of the crude product with authentic samples showed that the DBU method gave 50% starting material, 41% of the desired acetoxy acid, 7% of the hydroxy acid resulting from hydrolytic loss of the acetate group,[10] and 2% of the diene acid resulting from elimination of the acetate group. Based on the material allowed to react, reasonable selectivity (82%) was achieved.

Reagents such as lithium iodide in refluxing pyridine, 2,6-lutidine, or 2,4,6-collidine,[10] lithium iodide in hot dimethylformamide,[15] potassium *tert*-butoxide in DMSO,[11] and lithium ethyl mercaptide in hexamethylphosphoramide[14] have been developed for effecting cleavage of methyl esters by nucleophilic displacement of the carboxylate anion from the methyl group. Although DBU does not cleave esters under the mild conditions reported for the mercaptide[14] and potassium *tert*-butoxide methods,[11] this reagent does cleave methyl esters without the utilization of ionic nucleophilic reagents.

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Experimental Section

Melting points were obtained on a Fisher-Johns apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Nuclear magnetic resonance spectra were obtained using a Jeolco minimar spectrometer. Tetramethylsilane was used as an internal standard. Infrared spectra were obtained using a Perkin-Elmer Model 137 G spectrophotometer. Gas–liquid chromatography (glc) was performed using a Hewlett-Packard Model 402 gas chromatograph with a hydrogen flame detector. A glass column (6 ft × 0.25 in. o.d.) bent in a U shape and packed with 3% SE-30 on 100/120 mesh GCQ at a column temperature of 270° with a helium flow rate of 90 ml/min was used for all glc analyses.

Dehydrobromination–Decarbomethylation of Bromo Ketone 1.—Bromo ketone **1** (500 mg, 1.27 mmol) was added to a solution of 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) (390 mg, 2.56 mmol) and 1.51 ml of *o*-xylene. The temperature of the reaction solution was allowed to remain at 165° for 5 hr. The ether extract of the reaction mixture was acidified with 5% HCl and washed with 5% aqueous sodium carbonate and water, dried over anhydrous sulfate, and evaporated *in vacuo*. Crystallization of the residue from 20:1 methylene chloride–methanol solution yielded 299 mg (92%) of the white, crystalline compound **5**: mp 122.5–123.5° (lit.[16] mp 120–121°); λ_{max}^{KBr} 1650, 1600 cm^{-1}; δ^{CHCl_3} 1.41 (3 H, d, J = 6 cps), 1.73 (3 H), 4.33 (3 H), 6.91 (1 H, d, J = 1.8 cps), 7.39 (2 H, multiplet), 8.98 ppm (1 H, d, J = 9 cps). *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.90; H, 8.00.

Dehydrobromination of Bromo Ketone 1.—Bromo ketone **1** (500 mg, 1.27 mmol) was added to a solution of DBU (0.140 mg, 0.92 mmol) and 1.51 ml of *o*-xylene which was allowed to remain at 165° for 15 min. Following work-up in the manner described above, crystallization from aqueous methanol yielded 360 mg (90.5%) of the crystalline solid **3**: mp 175–177° (lit.[10] mp 173–175°); λ_{max}^{KBr} 1725, 1645, 1600, 1575 cm^{-1}; δ^{CHCl_3} 1.56 (3 H), 1.76 (3 H), 4.33 (3 H), 4.58 (3 H), 7.71 (1 H), 8.15 (2 H, multiplet), 9.58 ppm (1 H, d, J = 8 cps). *Anal.* Calcd for $C_{19}H_{22}O_4$: C, 72.50; H, 7.01. Found: C, 72.86; H, 7.14.

General Procedure for the *O*-Alkyl Cleavage of Methyl Esters. Methyl *O*-Methylpodocarpate, Methyl Mesitoate, and Methyl Triisophopylacetate, and Methyl Palmitate.—A solution of DBU (1.202 g, 8.30 mmol) and 0.83 mmol of the appropriate methyl ester was dissolved in 1.0 ml of *o*-xylene and the resulting mixture was allowed to remain at 165° for 48 hr. The usual work-up of the ether extract of the acidified carbonate layer yielded the corresponding acid, which was identical by ir, nmr, and mixture melting points with an authentic sample.

Attempted Cleavage of Acetate 9.—Acetate **9** (0.500 mg, 1.59 mmol) was dissolved in 1.9 ml of *o*-xylene and after the addition of DBU (2.42 g, 15.94 mmol) the solution was heated at 165° for 48 hr. The washed ether extract of the acidified reaction mixture yielded 0.489 mg (97.8%) of a white, crystalline material which was identical by glc, ir, nmr, and mixture melting points with an authentic sample of the starting material.

Selective Cleavage of Methyl 3β-Acetoxy-Δ^5-etienate.—Acetoxy ester (200 mg, 0.52 mmol) was added to a solution of DBU (740 mg, 4.86 mmol) in 0.62 ml of *o*-xylene and the resulting mixture was heated for 3.5 hr at 165°. The usual work-up yielded 154 mg of crude product. Glc comparison with authentic samples showed the product to be 50% of starting material, 41% of the desired acetoxy acid, 7% of the hydroxy acid resulting from hydrolytic loss of the acetate group, and 2% of the diene acid resulting from the loss of the acetate group.

Registry No.—**1**, 37931-64-9; **3**, 37931-65-0; **5**, 37931-66-1; DBU, 6674-22-2.

Acknowledgments.—We wish to thank the graduate school and the Biological and Physical Sciences Institute for partial financial support. We express our sincere appreciation to Dr. Ian K. Walker, Department of Scientific and Industrial Research, Wellington, New Zealand, for generous supplies of podocarpic acid.

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Synthesis of Benzo[*b*]-1,4-diazabicyclo[3.2.1]octane

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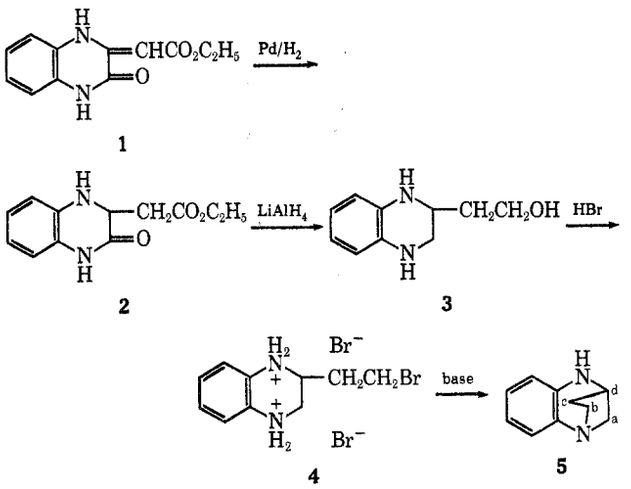
Benzo[*b*]1,4-diazabicyclo[3.2.1]octane (**5**), a new ring system, was prepared from 3-ethoxycarbonylmethylene-2-quinoxalone[1] as shown in Scheme I. Spectral data

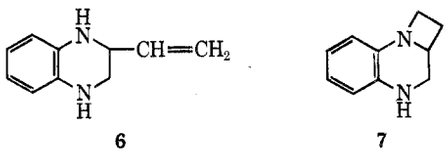
SCHEME I



support the keto structure shown above (**1**) rather than a tautomeric form. The infrared spectrum (KBr) shows conjugated ester carbonyl absorption at 1685 cm^{-1} and a lactam carbonyl at 1643 cm^{-1}, compared to the values 1705 and 1670 cm^{-1} for these bands in the dihydro compound **2**. The nmr spectrum of **1** (DMSO) showed a singlet at δ 5.55 which integrated for one proton. Protons on the α carbon atom of an α,β-unsaturated ester are known to absorb in this region.[2] Furthermore, no absorption was found in the region of δ 2.1 where protons in a methylene group adjacent to an ester group are known to absorb.[2] The uv spectrum (C_2H_5OH) was also in agreement with the assigned structure.

The free base corresponding to **4** could not be isolated due to the ease with which it undergoes cyclization to form **5**. The new compound (**5**) was formed by an intramolecular process as established by molecular weight determination.

Theoretically, two other compounds (**6** and **7**) might result from the treatment of compound **4** with bases.



6 **7**

Compound **6** was ruled out for two reasons. The infrared spectrum showed no alkene absorption. Further-

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