with 10% HCl, and then dried over $MgSO_4$. After filtration and vacuum removal of solvent, the residual oil was distilled in a bulb-to-bulb apparatus at 137 °C (0.15 mm) to give 5.0 g (86% yield) of a yellow oil: ^1H NMR ($CDCl_3$) δ 0.93 (d, 6 H, J = 7 Hz, $CH(CH_3)_2$), 2.0 (heptet, 1 H, J = 7 Hz, $CH(CH_3)$), 3.72 (d, 2 H, J = 7 Hz, CH_2CH), 3.8 (s, 2 H, $ClCH_2CO$)8 5.40 (AB q, 2 H, J = 8 Hz, NCH_2Cl), 6.7–7.6 (envelopes, 4 H, Ar H)

Anal. Calcd for $C_{13}H_{17}Cl_2NO_2$: C, 53.81; H, 5.91; N, 4.83. Cl, 24.43. Found: C, 53.85; H, 5.95; N, 4.83; Cl, 24.34.

Registry No. α-Chloro-*N*-(bromomethyl)-*N*-(2,6-dimethyl-1-cyclohexen-1-yl)acetamide, 81634-03-9; *N*-(methoxymethyl)-*N*-(2,6-dimethyl-1-cyclohexen-1-yl)chloracetamide, 78179-95-0; α-chloromethyl-*N*-(2,6-dimethyl-1-cyclohexen-1-yl)acetamide, 81634-02-8; *N*-(ethoxymethyl)-*N*-(2,6-dimethyl-1-cyclohexen-1-yl)chloroacetamide, 77117-40-9; α-chloro-2′-ethyl-6′-(trifluoromethyl)-*N*-(chloromethyl)acetanilide, 81634-12-0; α-chloro-2′-ethyl-6′-(trifluoromethyl)-*N*-(methoxymethyl)acetanilide, 80808-80-6; α-chloro-2′-isobutoxy-*N*-(chloromethyl)acetanilide, 81987-75-9; α-chloro-2′-isobutoxy-*N*-(methoxymethyl)acetanilide, 81987-76-0.

Synthesis of Catalpalactone

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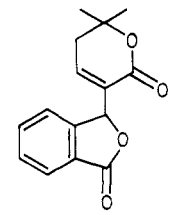
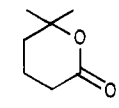
Catalpalactone, a dilactone of natural occurrence, is found in the heartwood of the tree *Catalpa ovata* G. Don, from which it was isolated by Nagakura and co-workers.[1] Later the same compound was encountered in the wood of a related species, *C. bignonioides* Walt.[2] The structure 1 for catalpalactone has been deduced on the basis of chemical behavior and spectroscopic properties.[1,2] Despite the presence of an asymmetric center in 1, the natural compound is optically inactive and presumably a racemate.

We envisaged a synthesis of catalpalactone via alkylation of δ,δ-dimethyl-δ-valerolactone (2) by a 3-substituted phthalide in which the substituent is a good leaving group. The lactone was obtained by reduction of commercial 5,5-dimethyl-2-pentenolactone, by Baeyer–Villiger oxidation of 2,2-dimethylcyclopentanone (3),[3] and from 2-methyl-3-buten-2-ol by ethyl cyanoacetate addition followed by hydrolysis and lactonization.[4] The Baeyer–Villiger reaction was expected to furnish the desired lactone on mechanistic grounds.[5] We first chose 3-bromophthalide (4), readily available by free-radical bromination of phthalide,[6] as alkylating agent. Exposure of it to the anion of δ,δ-dimethyl-δ-valerolactone in dry tetrahydrofuran afforded dihydrocatalpalactone (5) in 8% yield, the product having melting point and spectral properties identical with those reported;[1,2] an authentic sample was not available. Apparently this reaction was stereoselective, only one of the two possible racemates having been formed. No attempt was made to establish its stereochemistry, since the next step destroyed one of the centers of asymmetry. A greatly superior yield (78%) of 5 was obtained when 3-[(*p*-toluenesulfonyl)oxy]phthalide (6) was used as substrate.



1



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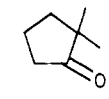

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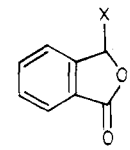

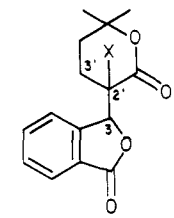

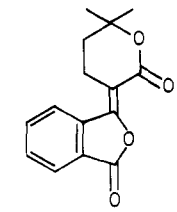

4, X = Br
6, X = $OSO_2C_6H_4CH_3(p)$

5, X = H
7, X = SePh

8

The dihydrocatalpalactone was next converted into its carbanion with lithium 2,2,6,6-tetramethylpiperidide. Because of the outcome of the synthetic sequence (see below) the carbanion center must be located at position 2′ rather than 3 in 5. The carbanion was reacted with diphenyl diselenide[7] to give, in 15% yield, 2′-(phenylseleno)dihydrocatalpalactone (7), along with considerable amounts of unreacted diselenide and lactone, presumably because of steric hindrance of the reaction. This product was subjected to elimination vis its selenoxide, by treatment with hydrogen peroxide. This gave, in quantitative yield from the selenide, catalpalactone (1), identical in every respect with an authentic sample. None of the isomeric product 8 was encountered, elimination having occurred exclusively via the 3′- rather than the 3-position in 7. This behavior was to be expected because elimination away from an electronegative atom (in this case oxygen) is generally preferred; further, the formation of an endocyclic rather an exocyclic double bond is favored.[8]

Experimental Section

Melting points and boiling points are uncorrected. UV and IR spectra were recorded on Perkin-Elmer 202 and 137 instruments, respectively. NMR spectra were measured on a JEOL FX-90Q instrument and mass spectra on a Hewlett-Packard 5840A GC/MS spectrometer. GC was conducted on an F and M Model 810 gas chromatograph.

3-[(*p*-Toluenesulfonyl)oxy]phthalide (6). 3-Bromophthalide was prepared by the free-radical bromination of phthalide,[6] in 73% yield. It crystallized from cyclohexane in plates: mp 74–78 °C (lit.[6] mp 78–80 °C); NMR ($CDCl_3$) δ 7.1 (s, 1 H, CHBr), 7.3–7.8 (m, 4 H, Ar H). This compound (2.13 g, 0.01 mol) and freshly prepared, dry silver *p*-toluenesulfonate[9] (2.79 g, 0.01 mol) in dry acetonitrile (50 mL) were stirred at 0 °C for 1 h and then filtered with the aid of Celite. The solvent was removed in vacuo, leaving a colorless syrup (3.05 g, 100%) which solidified readily and showed a single spot on TLC. It was used without further purification. 6: IR ($CHCl_3$) 1750 (C=O), 1390 (CSO_2OR) cm^{-1}; NMR ($CDCl_3$ + Me_2SO-d_6) δ 2.2 (s, 3 H, CH_3), 7.1 (s, 1 H, CHO), 7.0–7.8 (m, 4 H, Ar H). Attempts to make this compound by conventional tosylation of 3-hydroxyphthalide were unsuccessful owing to formation of di-3-phthalyl ether by tosylate displacement by the anion of the substrate.

δ,δ-Dimethyl-δ-valerolactone (2). A. Commercial 5,5-dimethyl-2-pentenolactone (0.89 g, 0.007 mol) in ethanol (75 mL) was shaken with 10% Pd–C catalyst (0.1 g) in hydrogen at at-

(1) Inouye, H.; Okuda, T.; Hirata, Y.; Nagakura, N.; Yoshizaki, M. *Tetrahedron Lett.* **1965**, 1261.
(2) Inouye, H.; Okuda, T.; Hirata, Y.; Nagakura, N.; Yoshizaki, M. *Chem. Pharm. Bull. Jpn.* **1967**, *15*, 786.
(3) Kessar, S. V.; Mahajan, K. P. *J. Indian Chem. Soc.* **1962**, *39*, 147.
(4) Surzur, J. M.; Teissier, P. *Bull. Soc. Chim. Fr.* **1970**, 653, 1611.
(5) Norman, R. O. C. "Principles of Organic Synthesis", 2nd ed.; Chapman and Hall: London, 1978; p 471.
(6) Koten, I. A.; Sauer, R. J. "Organic Syntheses", Collect. Vol. V; Wiley: New York, 1973; p 145.
(7) Cf. Grieco, P. A.; Miyashita, M. *J. Org. Chem.* **1974**, *39*, 120.
(8) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049.
(9) Cf. Hoffmann, H. M. R. *J. Chem. Soc.* **1965**, 6748.

0022-3263/82/1947-3171$01.25/0

mospheric pressure and temperature until 1 mol of gas had been absorbed. The solution was filtered and concentrated in vacuo, and the residue was distilled: bp 105 °C (2 mmHg); 0.89 g, 98%; IR (film) 1727 (C=O), 1206, 1140 cm^{-1} (CO); NMR ($CDCl_3$) δ 1.26 (s, 6 H, 2 CH_3), 1.4–1.8 (m, 4 H, CH_2CH_2), 2.2 (m, 2 H, CH_2CO).

B. By Baeyer–Villiger Oxidation of 2,2-Dimethylcyclopentanone. 2,2-Dimethylcyclopentanone was synthesized from 2-methylcyclohexanone.[3] Trifluoroperacetic acid was prepared by mixation of 85% hydrogen peroxide (1.0 mL) and trifluoroacetic anhydride (6.14 g, 0.030 mol) at 5–10 °C. After 90 min at 0 °C 2,2-dimethylcyclopentanone (3.36 g, 0.030 mol) was added portionwise with shaking and ice-cooling during 40 min. The mixture was kept at 0 °C overnight and then diluted with dichloromethane (50 mL) and poured into an excess of cold aqueous potassium carbonate. The layers were separated, and the aqueous layer was extracted twice with dichloromethane. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated at room temperature in vacuo. The residual lactone distilled at 105 °C (2 mmHg) (3.8 g, 99%); it was identical (IR and GC comparison) with the product prepared as in **A** above.

C. From 2-Methyl-3-buten-2-ol. The lactone was also prepared from ethyl cyanoacetate by free-radical addition to 3-buten-2-ol followed by alkaline hydrolysis and lactonization.[4] The product (60% overall yield) distilled at 105–107 °C (3–4 mmHg) and was identical with that prepared by procedures **A** and **B**.

Dihydrocatalpalactone (5). A. From 3-Bromophthalide. To diisopropylamine (0.395 g, 0.0039 mol) in dry tetrahydrofuran (10 mL) was added *n*-butyllithium (0.0039 mol) gradually, with stirring at −78 °C. The mixture was allowed to reach room temperature and stirred thereat for 30 min. It was then recooled to −78 °C and δ,δ-dimethyl-δ-valerolactone (0.5 g, 0.0039 mol) in dry tetrahydrofuran (10 mL) was added all at once. The solution was allowed to reach room temperature, then recooled to −78 °C, and treated with a solution of 3-bromophthalide (0.83 g, 0.0039 mol) in dry tetrahydrofuran (30 mL) with stirring. The red solution was allowed to arrive at room temperature, refluxed gently for 17.5 h, and then poured onto crushed ice and dilute HCl. The product was isolated with ether. It was chromatographed on silica gel (30 g) with elution with benzene. Evaporation of the eluates yielded dihydrocatalpalactone (0.081 g, 8%), which separated from methanol in plates, mp 154–155 °C (lit.[1,2] mp 153–154 °C). The IR spectrum was identical with the published spectra.[1,2]

B. From 3-[(*p*-Toluenesulfonyl)oxy]phthalide. To 2,2,6,6-tetramethylpiperidine (1.55 g, 0.011 mol) in dry tetrahydrofuran (5 mL) was added *n*-butyllithium (0.011 mol) at −78 °C, with stirring. The mixture was allowed to reach room temperature during 30 min, then recooled to −78 °C, and δ,δ-dimethyl-δ-valerolactone (1.20 g, 0.0094 mol) in dry tetrahydrofuran (10 mL) added. The cooling bath was removed and the mixture stirred for 30 min and then recooled to −78 °C. A solution of 3-[(*p*-toluenesulfonyl)oxy]phthalide (2.85 g, 0.0094 mol) in dry tetrahydrofuran (20 mL) was added all at once. After 1 h of stirring at −78 °C the mixture was poured onto crushed ice and dilute HCl and the product isolated with ether. The extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. A thick, orange syrup (2.73 g) remained; it was chromatographed on silica gel (60 g) with dichloromethane elution. Evaporation of the eluates afforded a very pale yellow syrup (1.90 g, 78%) which solidified readily. A small portion separated from methanol in plates, mp 154–155 °C, identical with the product from A above: IR (film) 1757 (C=O), 1704 (C=O), 1443, 1267, 1193 (CO), 1106 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.43 (s, 6 H, 2 CH_3), 1.2–1.9 (m, 4 H, CH_2CH_2), 3.0 (m, 1 H, CHCO), 6.36 (d, 1 H, CHO), 7.4–8.0 (m, 4 H, Ar H); mass spectrum, *m/e* 260 (M^+). Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.21; H, 6.20.

Catalpalactone (1). Lithium 2,2,6,6-tetramethylpiperidide (0.0019 mol) was prepared as described above at −78 °C and allowed to reach room temperature with stirring during 2 h. The solution was then recooled to −78 °C and a solution of dihydrocatalpalactone (0.325 g, 0.001 25 mol) and hexamethylphosphoric triamide (0.34 g, 0.0019 mol) in dry tetrahydrofuran (10 mL) was added rapidly, with stirring. After it had reached ambient temperature the mixture was treated with diphenyl diselenide (0.59 g, 0.0019 mol) in dry tetrahydrofuran (10 mL) rapidly. Reaction was allowed to proceed at room temperature for 30 min and then the whole was poured onto a mixture of crushed ice and dilute HCl. The product, isolated by 3-fold ether extraction, was a gum (0.94 g) which was chromatographed on silica gel (20 g) with elution in order by hexanes–chloroform (9:1, leading to unreacted diselenide, 0.45 g), 1:1 (leading to unreacted dihydrocatalpalactone, 0.25 g), and finally with chloroform to yield 2′-(phenylseleno)-dihydrocatalpalactone (7; 0.078 g, 15%; 63% based on unrecovered catalpalactone) used without further purification. This product (0.085 g, 0.2 mmol) was mixed with glacial acetic acid (2 drops), tetrahydrofuran (2 mL), and 30% hydrogen peroxide (0.3 mL), stirred at 0 °C for 30 min, and then poured into ice-cold aqueous sodium bicarbonate; the product was isolated with ether. In vacuo concentration of the dried extracts afforded a semisolid product, which was chromatographed on silica gel (3.5 g) and eluted with hexanes-chloroform (1:1). Evaporation yielded catalpalactone (1) which separated from methanol in plates, mp 106–107 °C (0.06 g, 100%), undepressed by admixture with an authentic sample (mp 105–106 °C). The IR, NMR, and UV spectra were identified with those of natural catalpalactone:[1,2] IR (film) 1760 (C=O), 1742 (C=O), 1447, 1267, 1107 cm^{-1}; NMR ($CDCl_3$) δ 1.3 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 2.5 (m, 2 H, CH_2), 6.4 (s, 1 H, CHO), 6.6–6.8 (t, J = 5 Hz, 1 H, =CH), 7.4–7.9 (m, 4 H, Ar H); UV λ_{max} (EtOH) 275 (log ϵ 3.20), 282 nm (3.20); mass spectrum, *m/e* 258 (M^+). Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46. Found: C, 69.61; H, 5.51.

Acknowledgment. We thank Dr. G. Agnès (Istituto Guido Donegani, Novara, Italy) for a gift of 5,5-dimethyl-2-pentenolactone, and Dr. N. Nagakura (Kobe Women's College of Pharmacy, Japan) for an authentic sample of catalpalactone. Mr. J. N. Herron we thank for the NMR spectra. The NMR spectrometer was purchased with funding provided by the National Science Foundation.

Registry No. 1, 1585-68-8; 2, 2610-95-9; 3, 4541-32-6; 4, 6940-49-4; 5, 1585-50-8; 6, 82027-09-6; 7, 82027-10-9; 5,5-dimethyl-2-pentenolactone, 19895-34-2; 2-methyl-3-buten-2-ol, 115-18-4.

A Partial Homo-Favorskii Rearrangement in the Diterpene Series

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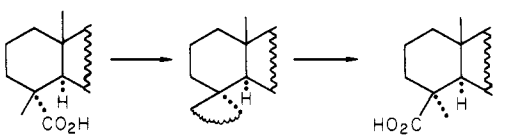
The inversion of a quaternary carbon site without scission of bonds attached thereto is an inherently difficult task. It was shown some time ago in the resin acid field that such a problem [e.g., the conversion of compounds of the dehydroabietic acid type (1) into those of the callistric acid form (2)] can be solved by functional group exchange via a ring formation–cleavage reaction sequence:[1]



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