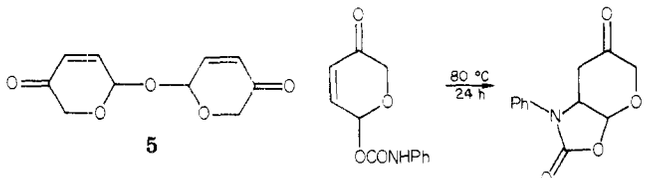
in the adducts in entries 2 and 4 as well as their relative proportions in the isolated adduct mixtures. While only one isomer formed in entry 5, the stereochemistry is not available from this probe.

Attempts to vary the conditions of the reaction offered no useful alternatives. With catalysis by boron trifluoride etherate at room temperature, no adduct formed from **4** and dimethyl acetylenedicarboxylate and the precursor **4** was slowly destroyed. In sulfuric or trifluoroacetic acid **4** rapidly turned black. On initiation with bases, precursor **4** at room temperature with triethylamine formed a dimer, the subject of the following paper.[6] Other derivatives of **3** with more active leaving groups were studied. Triflation of **3** at −78 °C (pyridine/CH_2Cl_2) produced an ether dimer **5**, implying rapid loss of triflate to an oxonium interme-



5 6 7

diate which rapidly added a second mole of alcohol **3**. The trifluoroacetate derivative of **3** could be formed at low temperatures but decomposed rapidly at ambient temperature, alone or in the presence of dienophiles, and yielded no adducts or other isolable products. In an attempt to create an acyl derivative which might intramolecularly remove the hydrogen necessary for enolization, we allowed **3** to react with dimethylcarbamoyl chloride and with phenyl isocyanate. In the former reaction a product could not be isolated, but the latter **6**, mp 139–140 °C, formed in 80% yield at room temperature in 6 h. On heating at 80 °C, however, **6** cyclized quantitatively to **7** mp 142–143 °C, which gave no adducts on being heated further with dimethyl acetylenedicarboxylate.

In summary, the precursor **4** proves to be an equivalent of the pyrylium zwitterion **1** for thermal cycloadditions to form ether-bridged cycloheptenones suitable for further synthetic elaboration with regio- and stereocontrol. The cycloaddition, which requires strongly activated dienophiles, proceeds with complete regiospecificity and with stereoselectivity heavily favoring the exo adduct.

Experimental Section

General. Infrared spectra were determined with a Perkin-Elmer Model 137 or 567 infrared spectrophotometer and mass spectra on an AE1 MS-12 spectrometer. ^1H NMR and decoupling experiments were performed on a Perkin-Elmer R-32 90-MHz spectrometer. Chemical shifts are reported in δ values relative to tetramethylsilane as an internal standard. The solvent, $CDCl_3$ or CD_3CN, was filtered through a short column of activity grade I basic alumina immediately before use. Sealed-tube reactions were performed in sealed thick-wall NMR tubes which were also wrapped in aluminum foil during heating. Only dipolarophiles which had been purified by recrystallization or distillation were employed.

Pyrolysis of 2-Acetoxy-1-oxacyclohex-3-en-5-one (4) with Acrolein. The synthesis of 6-formyl-8-oxabicyclo[3.2.1]oct-3-en-2-one (entry 4, Table I) is representative. Pyranose acetate **4**[2] (59.7/mg, 0.38 mmol) was dissolved in 0.35 mL of $CDCl_3$ contained in a pyrolysis tube. To this solution was added 21.3 mg (0.38 mmol) of acrolein. The tube was sealed and placed in an oil bath maintained at ~134 °C for 13 h. Preparative TLC on silica gel with diethyl ether/ethyl acetate (6:5) as eluant (two elutions) afforded 39.9 mg (69% yield) of 6-*exo*-formyl-8-oxabicyclo[3.2.1]oct-3-en-2-one [NMR ($CDCl_3$), Table I; IR ($CHCl_3$) 1740, 1690 cm^{-1}] and the 6-endo isomer [NMR ($CDCl_3$) δ 9.82 (CHO, d, J = 2 Hz)] in a ratio of 4:1, respectively.

The other adducts were prepared in the same way, with yields and data shown in Table I. All showed the characteristic IR band of unsaturated ketone at 1690 ± 10 cm^{-1}.

Registry No. **3**, 35436-57-8; **4**, 62644-49-9; **5**, 65746-82-9; **6**, 74019-32-2; **7**, 74019-33-3; butynedioic acid dimethyl ester, 762-42-5; 2,5-furandione, 108-31-6; 1-(ethenylsulfonyl)-1,1,2,2,3,3,4,4,4-nonafluorobutane, 71561-58-5; 2-propenal, 107-02-8; 2-methyl-2-propenal, 78-85-3; 6,7-dicarbomethoxy-8-oxabicyclo[3.2.1]oct-3,6-dien-2-one, 74019-34-4; *endo*-4,8-epoxy-3a,4,8,8a-tetrahydrocyclohepta[*c*]furan-1,3,7-trione, 74019-35-5; *exo*-4,8-epoxy-3a,4,8,8a-tetrahydrocyclohepta[*c*]furan-1,3,7-trione, 74080-22-1; *exo*-6-nonafluorobutylsulfonyl-8-oxabicyclo[3.2.1]oct-3-en-2-one, 74019-36-6; *endo*-6-formyl-8-oxabicyclo[3.2.1]oct-3-en-2-one, 74019-37-7; *exo*-6-formyl-8-oxabicyclo[3.2.1]oct-3-en-2-one, 74019-38-8; 6-formyl-6-methyl-8-oxabicyclo[3.2.1]oct-3-en-2-one, 74019-39-9; dimethylcarbamoyl chloride, 79-44-7; phenyl isocyanate, 103-71-9.

(6) J. B. Hendrickson and J. S. Farina, *J. Org. Chem.*, following paper in this issue.

A Simple Synthesis of Eight- and Ten-Membered Carbocyclic Rings[1]

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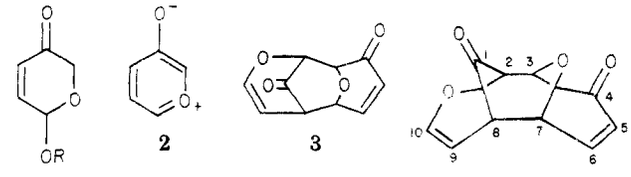
Received January 30, 1980

In the course of studies on the cycloadditions of **2** formed from **1** (R = Ac) by pyrolysis,[2] we could not isolate any products on heating in the absence of dienophile. However, when **1** (R = Ac) was treated at room temperature with triethylamine, it was transformed into the isomeric dimer **3**, mp 143–147 °C (mass spectrum, m/e 192 (M^+)) in 68% yield. The infrared spectrum showed carbonyl peaks at 1770 (5.65 μm) and 1690 cm^{-1} (5.92 μm), consistent with **3**. The stereostructure **4** for this doubly



1 2 3 4

bridged eight-membered ring was assigned by NMR decoupling experiments at 270 MHz.[3] The coupling constants for the two pairs of bridgehead protons are $J_{2,3}$ = 8.8 Hz and $J_{7,8}$ = 9.4 Hz. These are consistent with the dihedral angles of 0 °C expected[4] for the central boat ring (1–2–3–O–7–8) in **4**, whereas an analogous dimer of 3-oxypyridinium, formulated with a chair central ring,[5] showed the expected coupling constant of $J \simeq 2$ Hz. Furthermore, no possible dimer of **2** can exhibit more than

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) J. B. Hendrickson and J. S. Farina, *J. Org. Chem.*, preceding paper in this issue.

(3) Spectra were taken on Professor A. Redfield's 270-Hz NMR spectrometer, funded by the National Institutes of Health Grant GM 20168 and the Research Corporation. The assistance of David Harris for decoupling experiments is gratefully acknowledged.

(4) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); S. Sternhell, *Q. Rev., Chem. Soc.*, **23**, 236 (1969).

(5) N. Dennis, B. Ibrahim, and A. R. Katritzky, *J. Chem. Soc., Perkin Trans. 1*, 2296, 2307 (1976).

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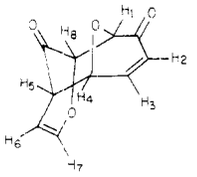
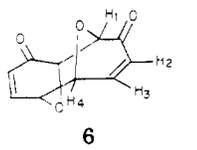
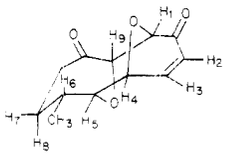
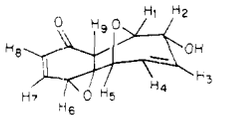
Table I. NMR Analysis of the Products[a]

products	δ values (J, Hz)	
 4	H_1, 5.02 (8.8)	H_5, 3.63 (9.4, 7.3, 2.6)
	H_2, 6.30 (10.3)	H_6, 4.71 (7.3, 5.6)
	H_3, 7.17 (10.3, 5)	H_7, 6.42 (5.6)
	H_4, 5.26 (9.4, 5)	H_8, 4.78 (8.8, 2.6)
 6	H_1, 4.07 (s)	
	H_2, 6.37 (10)	
	H_3, 7.34 (10, 5)	
	H_4, 4.38 (5)	
 9	H_1, 4.01 (s)	H_6, 2.50 (9, 7, 6, 3)[a]
	H_2, 6.38 (10)	H_7, 2.79 (15, 6)
	H_3, 7.16 (10, 5)	H_8, 2.64 (15, 9)
	H_4, 4.33 (5)	H_9, 4.24 (s)
	H_5, 3.57 (3)	CH_3, 1.37 (7)[a]
 11	H_1, 3.76 (6.8)[a]	H_6, 4.17 (4.5, 1)
	H_2, 4.56 (6.8, M, ~2)[a]	H_7, 7.27 (10.1, 4.5)
	H_3, 6.13 (10, 2, 1.2)	H_8, 6.31 (10.1)
	H_4, 5.93 (10, 3.5, 2.3)	H_9, 4.35 (s)
	H_5, 3.98 (3.5, 1.2, 1)	

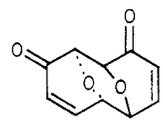
[a] Irradiation for decoupling.

six pairs of adjacent protons, but dimer **3** has seven coupling constants. The stereostructure **4** is, however, perfectly oriented for a W coupling (2–8) and such a coupling of $J = 2.6$ Hz appears (see the analysis in Table I) in which all the coupling constants are consistent with the dihedral angles seen on the model.

The dimer **3** could be prepared more simply by treating the alcohol **1** (R = H) with trifluoroacetic anhydride and triethylamine in methylene chloride at −78 °C and then adding a second mole of the base before warming to room temperature. When the aqueous workup was slightly acidic, a second product was observed by NMR, apparently the hydrate (at C-10) of the enol ether of **3**. This cyclic acetal implies the synthetic possibility of releasing the cyclized enol ether as a free acetaldehyde side chain for further elaboration to eight-membered-ring target molecules. However, we have not explored this further conversion since our interest focused on the isomerization of dimer **3**.

Upon heating dimer **3** at 140 °C for 7 h it was transformed into an isomer, mp 200–206 °C. Pyrolysis of **3** or the new isomer in the presence of dimethyl acetylenedicarboxylate at 135 °C for 17 h or up to 200 °C for 10 h gave only a trace of the cycloaddition previously observed with **1** (R = Ac).[2] This implies that the isomerization does not proceed by cracking the dimer to **2** and redimerizing.[6] The isomer was assigned structure **5** from its spectra, which showed a single carbonyl peak in the infrared at 1690 cm^{-1} (5.92 μm) and a simple NMR of four equal peaks (Table I). The implicit symmetry is unique to the stereostructure

(6) The analogous oxypyridinium dimer of Katritzky,[5] with inverted stereochemistry, is easily cracked thermally to yield monomer for other cycloadditions.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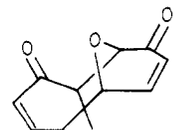
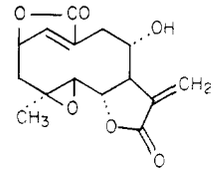
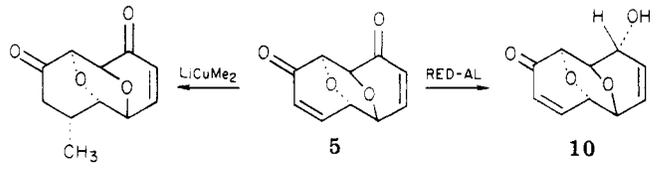

6

6 with two equivalent halves; also this structure can arise simply by breaking bond 7–8 in **4** and remaking bond 7–10 in the pyrolysis, without necessitating a complete cracking to **2**.

The establishment of **5** creates a singular opportunity for synthetic elaboration of sesquiterpenes with the germacrane skeleton (cf., elephantol (**7**,))[7] since it possesses not only the requisite ten-membered carbocycle of that skeleton but also a structure rigidified by ether bridges for good stereocontrol. Similar bicyclic structures generally exhibit clear stereospecificity for the exo approach of reagents. Furthermore, the ether bridges can presumably be opened by zinc reduction to afford hydroxyl groups of known configuration. To take advantage of this opportunity, however, requires independent manipulation of the duplicated functionality on the two halves as well as a demonstration of exo stereospecificity. As a test of this selectivity, we tried two reactions useful for the elaboration to germacranolides like **7**.

In the first, **5** was treated with equimolar lithium dimethylcuprate and gave cleanly only a single product **8**


7



8 5 10

with two carbonyl peaks in the IR spectrum at 1730 cm^{-1} (5.78 μm) and 1690 cm^{-1} (5.92 μm). The NMR spectrum is fully consistent with stereostructure **9** as detailed in Table I. In the second test, **5** was reduced with 0.5 equiv of Red-Al ($NaAlH_2(OCH_2CH_2OCH_3)_2$) and again afforded only one reduction product, formulated as **10** from its spectra. The NMR spectrum, tabulated in Table I, is fully consistent with the expected stereostructure **11**. In these structures the protons at the paired bridgeheads lie close to a 90° dihedral angle and show no coupling.

From these tests it is clear that the symmetrical halves can be chemically distinguished, paving the way for further synthetic explorations to ten-membered-ring targets. The germacranolides (cf., **7**) all have trans γ-lactones, introducible in principle by Claisen rearrangement of **10** with ortho-acetate.[8] This reaction has not yet succeeded, apparently owing to steric hindrance on the underside (cf., **11**) but can be undertaken later after opening the ether bridge.

(7) S. M. Kupchan, Y. Aynehehi, J. M. Cassady, A. T. McPhail, G. A. Sim, H. K. Schnoes, and A. L. Burlingame, *J. Am. Chem. Soc.*, **88**, 3674 (1966).

(8) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, Tsung-ti Lee, D. J. Faulkner, and M. R. Peterson, *J. Am. Chem. Soc.*, **92**, 741 (1970).

In summary, the oxypyrylium zwitterion appears to be a versatile synthon for cycloaddition to seven-,[2] eight- and ten-membered carbocyclic rings. Furthermore, the synthetic value of the initial adducts lies in their multiple functionality and the ether-bridged rigidity for stereocontrol, as demonstrated by the test reactions reported here.

Experimental Section

General. Details are described in the preceding paper.[2] Elemental analysis was performed by Galbraith Laboratories, Inc., Knoxville, TN. Dichloromethane (from phosphorus pentoxide) and tetrahydrofuran (from lithium aluminum hydride) were distilled prior to use under nitrogen.

Synthesis of 3,12-Dioxatricyclo[5.3.1.1.^{2,6}]dodeca-4,8-diene-10,11-dione (3). A. From Pyranose 1 (R = $COCH_3$). To a rapidly stirred dichloromethane (20 mL) solution of 2-acetoxy-1-oxacyclohex-3-en-5-one[9] (1, R = $COCH_3$, 1.6 g, 10.2 mmol) at 0 °C under a nitrogen atmosphere was added an equimolar amount of triethylamine. After warming to room temperature over 3 h, it was stirred overnight. Concentration under reduced pressure, followed by column chromatography on silica gel with dichloromethane/ethyl acetate (6:1), gave 675 mg (69% yield) of dimer 3 as a white solid: mp 143–147 °C; NMR (CD_3CN–Me_2SO-d_6), Table I; IR ($CDCl_3$) 1770, 1690 cm^{-1}; mass spectrum, m/e 192 (M^+).

B. From Pyranose 1 (R = $COCF_3$). To 113.6 mg (1 mmol) of pyranose 1 (R = H)[9] in dichloromethane (3 mL) at −78 °C under a nitrogen atmosphere was added 0.14 mL (1 mmol) of triethylamine. This solution was added to 0.14 mL (1 mmol) of trifluoroacetic anhydride in 2 mL of dichloromethane at −78 °C via a double tipped cannula. After 15 min, 0.14 mL (1 mmol) of triethylamine was added dropwise to the above reaction mixture. The resulting solution was warmed to −10 °C over 5.5 h and then concentrated in vacuo. The residue was dissolved in ethyl acetate, washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure gave 62.8 mg (66% yield) of dimer 3.

Synthesis of 11,12-Dioxatricyclo[5.3.1.1.^{2,6}]dodeca-4,8-diene-3,10-dione (5). A chloroform solution (1 mL) of dimer 3 (203 mg, 1.04 mmol) was sealed into a dried pyrolysis tube and then immersed for 7 h in an oil bath maintained at ~141 °C. After cooling, the heterogeneous reaction mixture was filtered through Celite. Upon concentration of the filtrate in vacuo, 169 mg (83% yield) of dimer 5 was obtained. Column chromatography on silica gel with dichloromethane/ethyl acetate (6:1) afforded pure dimer 5 as a white solid, mp 200–205 °C. Dimer 5 could also be prepared by refluxing dimer 3 in xylene under a nitrogen atmosphere overnight. Removal of the solvent under reduced pressure and chromatography as above gave pure dimer 5: NMR (CD_3CN), Table I; IR (CH_2Cl_2) 1690 cm^{-1}; mass spectrum, m/e 192 (M^+). Anal. Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.63; H, 4.23.

Synthesis of 8-Methyl-11,12-dioxatricyclo[5.3.1.1^{2,6}]dodec-4-ene-2,10-dione (8). A 0.084 M THF solution of lithium dimethylcuprate (prepared by adding 0.58 mL of 2.87 M methyllithium–ether solution to 171.8 mg (0.84 mmol) of cuprous bromide–dimethyl sulfide complex[10] in 10 mL of anhydrous THF at −70 °C) was added to 160.6 mg (0.84 mmol) of dimer 5 in THF (10 mL) at −70 °C under a nitrogen atmosphere. After 1.5 h, the cloudy yellow reaction mixture was removed from the low-temperature bath and immediately quenched with 5 mL of saturated NH_4Cl solution. This mixture was taken up in ether (70 mL) and washed with saturated NH_4Cl solution until the aqueous layer was colorless. The organic extract was washed with brine (30 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Preparative TLC on silica gel using dichloromethane/ethyl acetate (10:1) as eluant gave 73.2 mg (42% yield) of 8 as a white solid: mp 120–124 °C; NMR ($CDCl_3$), Table I; IR ($CDCl_3$) 1730, 1690 cm^{-1}; mass spectrum, m/e 208 (M^+).

Synthesis of 10-Hydroxy-11,12-dioxatricyclo[5.3.1.1^{1,6}]dodeca-4,8-dien-3-one (10). To a cold (−78 °C) THF (9 mL) solution of dimer 5 (84.6 mg, 0.44 mmol) was added dropwise a solution of sodium aluminum bis(methoxyethoxy) dihydride in THF (1.65 mL, 0.133 M) under a nitrogen atmosphere. After the reaction mixture was warmed to 15 °C over 3 h, it was quenched with 5 mL of saturated NH_4Cl solution. A minimum amount of water was added to dissolve the resulting precipitate. This mixture was then extracted with ethyl acetate. The combined organic extracts were washed with saturated NH_4Cl solution, water, and brine and dried over anhydrous $MgSO_4$. Removal of the volatiles under reduced pressure afforded 74.1 mg of gummy solid. Preparative TLC on silica gel using dichloromethane/ethyl acetate (6:1) as eluant gave 11.2 mg (13% yield) of dimer 5 and 22.2 mg (26% yield) of keto alcohol 10: NMR (CD_3CN), Table I; IR ($CDCl_3$) 1690 cm^{-1}; mass spectrum, m/e 194 (M^+).

Registry No. 1 (R = Ac), 62644-49-9; 1 (R = H), 35436-57-8; 1 (R = $COCF_3$), 74036-55-8; 3, 74036-56-9; 5, 74036-57-0; 8, 74036-58-1; 10, 74036-59-2; lithium dimethylcuprate, 15681-48-8.

(9) O. Achmatowicy, Jr., P. Bukowski, B. Szechner, Z. Zwierzchowska, and A. Zamojski, *Tetrahedron*, 27, 1973 (1971).
(10) H. O. House, C. Y. Chu, J. M. Wilkins, and M. J. Umen, *J. Org. Chem.*, 40, 1460 (1975).

Base-Catalyzed Rearrangement of 4-Methyl-4-acetoxy-2,6-di-*tert*-butyl-2,5-cyclohexadienone

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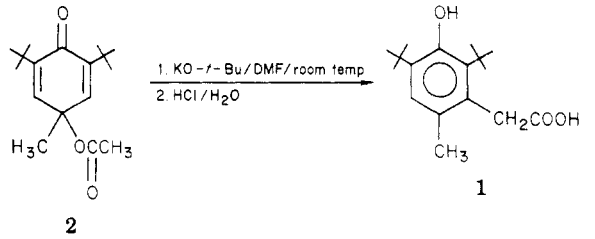
Received March 6, 1980

Recently, Nishinaga and co-workers[1] reported the synthesis of 1 by the rearrangement of 2 using potassium *tert*-butoxide (4:1 KO-*t*-Bu–2) in dimethylformamide, followed by acidification with aqueous hydrochloric acid. Compound 1 would be a very useful appendage in the synthesis of new antioxidants.[2] Our attempts to reproduce this work led to some interesting mechanistic observations.



2 1

When the rearrangement of 2 was carried out by using ≥2:1 potassium KO-*t*-Bu–2, 1 was isolated as reported.[1] However, when 1:1 KO-*t*-Bu–2 was used, there was isolated (50% yield) a white crystalline solid, mp 169–171 °C (CCl_4). (Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.24; H, 9.41), whose IR spectrum (KBr) exhibited absorptions at 1671 (α,β-unsaturated ketone) and 1762 cm^{-1} (five-membered lactone).[3] The ^1H NMR ($CDCl_3$) exhibited absorptions at 1.07 (s, 9 H), 1.17 (s, 9 H), 1.67 (s, 3 H), 6.12 (d, J = 2.0 Hz, 1 H), and 1.92–3.00 (m, 4 H) ppm downfield from internal Me_4Si. These values are clearly inconsistent with those values reported for 1 by Nishinaga and co-workers.[1]

The ^{13}C NMR spectrum was most revealing. Obtained under proton-decoupled conditions, 13 different carbon atoms were observed. However, under off-resonance conditions, seven of the carbon resonances exhibited cou-

(1) Nishinaga, A.; Itahara, T.; Hibi, M.; Matsuura, T. *Synthesis* **1976**, 554.
(2) Spivack, J. D.; Dexter, M. U.S. Patent 3 988 363, 1976.
(3) Nakanishi, K. "Infrared Absorption Spectroscopy"; Holden-Day: San Francisco, 1962; pp 42, 44.

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